

CYCLOPENTENE COMPOUNDS

This invention relates to cyclopentene compounds, to processes for their preparation, to pharmaceutical compositions containing them and to their use in medicine, in particular 5 their use in the treatment of conditions mediated by the action of PGE₂ at EP₁ receptors..

The EP₁ receptor is a 7-transmembrane receptor and its natural ligand is the prostaglandin PGE₂. PGE₂ also has affinity for the other EP receptors (types EP₂, EP₃ and EP₄). The EP₁ receptor is associated with smooth muscle contraction, pain (in particular 10 inflammatory, neuropathic and visceral), inflammation, allergic activities, renal regulation and gastric or enteric mucus secretion. We have now found a novel group of compounds which bind with high affinity to the EP₁ receptor.

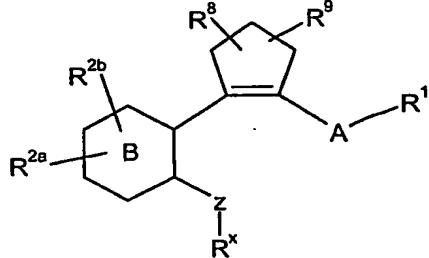
A number of review articles describe the characterization and therapeutic relevance of the 15 prostanoid receptors as well as the most commonly used selective agonists and antagonists: *Eicosanoids; From Biotechnology to Therapeutic Applications*, Folco, Samuelsson, Maclof, and Velo eds, Plenum Press, New York, 1996, chap. 14, 137-154 and *Journal of Lipid Mediators and Cell Signalling*, 1996, 14, 83-87 and *Prostanoid Receptors, Structure, Properties and Function*, S Narumiya et al, *Physiological Reviews* 1999, 79(4), 1193-126. An 20 article from *The British Journal of Pharmacology*, 1994, 112, 735- 740 suggests that Prostaglandin E₂ (PGE₂) exerts allodynia through the EP₁ receptor subtype and hyperalgesia through EP₂ and EP₃ receptors in the mouse spinal cord. Furthermore an article from *The Journal of Clinical Investigation*, 2001, 107 (3), 325 shows that in the EP₁ knock-out mouse 25 pain-sensitivity responses are reduced by approximately 50%. Two papers from *Anesthesia and Analgesia* have shown that (2001, 93, 1012-7) an EP₁ receptor antagonist (ONO-8711) reduces hyperalgesia and allodynia in a rat model of chronic constriction injury, and that (2001, 92, 233-238) the same antagonist inhibits mechanical hyperalgesia in a rodent model 30 of post-operative pain. S. Sarkar et al in *Gastroenterology*, 2003, 124(1), 18-25 demonstrate the efficacy of EP₁ receptor antagonists in the treatment of visceral pain in a human model of hypersensitivity. Thus, selective prostaglandin ligands, agonists or antagonists, depending 35 on which prostaglandin E receptor subtype is being considered, have anti-inflammatory, antipyretic and analgesic properties similar to a conventional non-steroidal anti-inflammatory drug, and in addition, inhibit hormone-induced uterine contractions and have anti-cancer effects. These compounds have a diminished ability to induce some of the mechanism-based side effects of NSAIDs which are indiscriminate cyclooxygenase inhibitors. In particular, the 40 compounds have a reduced potential for gastrointestinal toxicity, a reduced potential for renal side effects, a reduced effect on bleeding times and a lessened ability to induce asthma attacks in aspirin-sensitive asthmatic subjects. Moreover, by sparing potentially beneficial prostaglandin pathways, these agents may have enhanced efficacy over NSAIDS and/or COX-2 inhibitors.

In The American Physiological Society (1994, 267, R289-R-294), studies suggest that PGE₂-induced hyperthermia in the rat is mediated predominantly through the EP₁ receptor.

WO 96/06822 (March 7, 1996), WO 96/11902 (April 25, 1996), EP 752421-A1 (January 08, 1997), WO 01/19814 (22 March 2001), WO 03/084917 (16 October 2003), WO 03/101959 (11 December 2003) and WO 2004/039753 (13 May 2004) disclose compounds as being useful in the treatment of prostaglandin mediated diseases.

It is now suggested that a novel group of cyclopentene derivatives surprisingly are selective for the EP₁ receptor over the EP₃ receptor, and are therefore indicated to be useful in treating conditions mediated by the action of PGE₂ at EP₁ receptors. Such conditions include pain, or inflammatory, immunological, bone, neurodegenerative or renal disorders.

Accordingly the present invention provides cyclopentene compounds of formula (I):



(I)

wherein:

A represents an optionally substituted aryl, or an optionally substituted 5- or 6- membered heterocycl ring, or an optionally substituted bicyclic heterocycl group;

B represents a phenyl or pyridyl ring;

Z represents O, S, SO, or SO₂;

R¹ represents CO₂H, CN, CONR⁵R⁶, CH₂CO₂H, optionally substituted SO₂alkyl, SO₂NR⁵R⁶, NR⁵CONR⁵R⁶, COalkyl, 2H-tetrazol-5-yl-methyl, optionally substituted bicyclic heterocycle or optionally substituted heterocycl;

R^{2a} and R^{2b} each independently represents hydrogen, halo, optionally substituted alkyl, optionally substituted alkoxy, CN, SO₂alkyl, SR⁵, NO₂, optionally substituted aryl, CONR⁵R⁶ or optionally substituted heteroaryl;

R^x represents optionally substituted alkyl wherein 1 or 2 of the non-terminal carbon atoms are optionally substituted by a group independently selected from NR⁴, O and SO_n,

wherein n is 0, 1 or 2; optionally substituted alkenyl; or optionally substituted alkynyl; or R^x represents optionally substituted alkenyl, optionally substituted CQ^aQ^b-heterocycl, optionally substituted CQ^aQ^b-bicyclic heterocycl or optionally substituted CQ^aQ^b-aryl;

R⁴ represents hydrogen or an optionally substituted alkyl;

R⁵ represents hydrogen or an optionally substituted alkyl;

R⁶ represents hydrogen or optionally substituted alkyl, optionally substituted heteroaryl, optionally substituted SO₂aryl, optionally substituted SO₂alkyl, optionally substituted SO₂heteroaryl, CN, optionally substituted CQ^aQ^baryl, optionally substituted CQ^aQ^bheteroaryl or COR⁷;

5 R⁷ represents hydrogen, optionally substituted alkyl, optionally substituted heteroaryl or optionally substituted aryl;
R⁸ and R⁹ each independently represents hydrogen, chloro, fluoro, CF₃, C₁₋₃alkoxy or C₁₋₃alkyl;
Q^a and Q^b are each independently selected from hydrogen and CH₃;

10 wherein when A is a 6-membered ring the R¹ substituent and cyclopentene ring are attached to carbon atoms 1,2-, 1,3- or 1,4- relative to each other, and when A is a five-membered ring or bicyclic heterocycl group the R¹ substituent and cyclopentene ring are attached to substitutable carbon atoms 1,2- or 1,3- relative to each other;
and derivatives thereof.

15 When A is a six membered ring, preferably R¹ is attached to the group A in the 3 position relative to the bond attaching A to the cyclopentene ring.

20 Suitable examples of A include phenyl, pyridyl, pyridazinyl, pyrimidinyl and pyrazinyl, all of which may be optionally substituted.

Optional substituents for A include up to four substituents, preferably 0 or 1 substituent, independently selected from halogen, optionally substituted C₁₋₄alkyl e.g. CF₃, CH₃, and C₂H₅, NH₂, NHC₁₋₄alkyl, NHCOC₁₋₄alkyl, and SCH₃.

25 When B is pyridyl, in one aspect the pyridine N atom is situated adjacent to the ring carbon carrying the Z substituent.

Preferably Z is O.

30 Suitably R¹ includes CO₂H and CONHSO₂phenyl.

Particular examples of R^{2a} and R^{2b} include hydrogen, halogen, optionally substituted C₁₋₆alkyl e.g. CF₃ or CH₃, and optionally substituted C₁₋₆alkoxy.

35 Preferably R^{2a} is hydrogen or CH₃. More preferably R^{2a} is hydrogen.
Preferably R^{2b} represents hydrogen, halogen, CF₃, or CH₃.

40 Preferably R^{2b} is positioned 1,4- relative to the Z substituent and 1,3- relative to the cyclopentene ring.

Suitably R⁴ includes hydrogen and C₁₋₄alkyl.

Suitably R⁵ includes hydrogen or C₁₋₄alkyl.

5 Suitably R⁶ includes hydrogen, C₁₋₄alkyl or SO₂phenyl.

Suitably R⁷ include hydrogen or C₁₋₄alkyl.

Suitably R⁸ include CH₃ or hydrogen, in one aspect R⁸ represents hydrogen.

10

An example of R⁹ is hydrogen.

An example of Q^a is hydrogen.

15

An example of Q^b is hydrogen.

Suitably R^x includes optionally substituted C₁₋₈alkyl, optionally substituted C₂₋₈alkenyl and CH₂phenyl optionally substituted by one, two or three substituents, selected from Cl, Br, F, CF₃, OCF₃, C₁₋₄alkyl, and OC₁₋₄alkyl.

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In one aspect R^x is optionally substituted C₃₋₈alkyl, optionally substituted C₃₋₈alkenyl and CH₂phenyl optionally substituted by one, two or three substituents, selected from Cl, Br, F, CF₃, OCF₃, C₁₋₄alkyl, and OC₁₋₄alkyl.

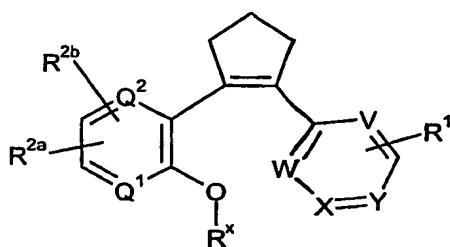
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Suitably R^x when an optionally substituted C₃₋₈alkyl includes e.g. isobutyl, CH₂cyclopentene and CH₂cyclohexene.

Suitably R^x when an optionally substituted C₂₋₈alkenyl include e.g. CH₂CH=CH₂ and CH₂CH=CH-phenyl.

30

A certain group of compounds of formula (I) are compounds of formula (IA):



(IA)

wherein:

35 W, X, and Y each represent CR¹² or N;

V represents CR¹, CR¹² or N;

wherein at least two of W, X, Y and V is CR¹², and R¹² is independently selected from hydrogen, halogen, CF₃, CH₃, NH₂, NHC₁₋₆alkyl, NHCOC₁₋₆alkyl, and SCH₃;

Q¹ and Q² each represents CH, or one of Q¹ and Q² is N and the other is CH;

5 R¹ is CO₂H, CONR⁵R⁶, CH₂CO₂H, SO₂C₁₋₆alkyl, SO₂NR⁵R⁶, NR⁵CONR⁵R⁶, tetrazolyl or COSO₂NR⁵R⁶;

R^{2a} and R^{2b} are selected from hydrogen, halogen, optionally substituted C₁₋₆alkyl, and optionally substituted C₁₋₆alkoxy;

R^x represents optionally substituted C₃₋₈alkyl, optionally substituted C₃₋₈alkenyl, and

10 optionally substituted CH₂phenyl;

R⁵ is hydrogen or C₁₋₄alkyl;

R⁶ is hydrogen, C₁₋₄alkyl or SO₂phenyl;

R¹² is selected from hydrogen, halogen, NR⁵R⁶, NR⁵COC₁₋₆alkyl, NR⁵SO₂C₁₋₆alkyl, OR⁵, SR⁵, and optionally substituted C₁₋₆alkyl;

15 or derivatives thereof.

Suitably R¹ includes CO₂H and CONHSO₂phenyl.

Suitably R^x includes optionally substituted C₃₋₈alkyl, optionally substituted C₃₋₈alkenyl, and

20 CH₂phenyl optionally substituted by one, two or three substituents, selected from Cl, Br, F, CF₃, OCF₃, C₁₋₄alkyl, and OC₁₋₄alkyl.

In one aspect R¹ is positioned 1,3-relative to the cyclopentene ring.

25 In another aspect one or two of W, X, Y and V is N.

In yet another aspect one of Q¹ and Q² is N and the other is CH.

A particular set of compounds are those wherein one or two of W, X, Y and V is N and Q¹

30 and Q² are both CH. A further set of compounds are those where one of Q¹ and Q² is N and W, X, Y, and V are each CR¹².

In one aspect Q¹ is N or CH and Q² is CH.

35 Suitably R^{2a} is hydrogen.

Suitably R^{2b} is positioned 1,4-relative to OR^x and 1,3-relative to the cyclopentene ring.

Suitably R^{2b} is selected from hydrogen, F, Br, Cl, CH₃ and CF₃.

40 Suitably R¹² includes hydrogen, halogen e.g. F or Cl, CF₃, NH₂, NHCOC₁₋₄alkyl, SCH₃, and C₁₋₄alkyl, e.g. CH₃ and C₂H₅;

Compounds of formula (I) include the compounds of Examples 1 to 417 and derivatives thereof.

5 A particular group of compounds of formula (I) include the compounds of Examples 145-148, 213-241, 342-368, and 388-417 and derivatives thereof.

The compounds of the invention are selective for EP₁ over EP₃. The compounds of the examples are at least 20 fold selective. Preferred compounds are at least 100 fold

10 selective for EP₁ over EP₃.

Derivatives of the compounds of formula (I) include pharmaceutically acceptable derivatives.

The term "pharmaceutically acceptable derivative" means any pharmaceutically acceptable salt, solvate, ester, or solvate of salt or ester of the compounds of formula (I),

15 or any other compound which upon administration to the recipient is capable of providing (directly or indirectly) a compound of formula (I).

It will be appreciated by those skilled in the art that the compounds of formula (I) may be modified to provide pharmaceutically acceptable derivatives thereof at any of the functional

20 groups in the compounds, and that the compounds of formula (I) may be derivatised at more than one position.

It will be appreciated that, for pharmaceutical use, the salts referred to above will be pharmaceutically acceptable salts, but other salts may find use, for example in the

25 preparation of compounds of formula (I) and the pharmaceutically acceptable salts thereof.

Pharmaceutically acceptable salts include those described by Berge, Bighley and Monkhouse, *J. Pharm. Sci.*, 1977, 66, 1-19. The term "pharmaceutically acceptable salts"

refers to salts prepared from pharmaceutically acceptable bases including inorganic bases and organic bases. Salts derived from inorganic bases include aluminum, ammonium, calcium,

30 copper, ferric, ferrous, lithium, magnesium, manganic salts, manganous, potassium, sodium, zinc, and the like. A particular salt is the sodium salt. Salts derived from pharmaceutically acceptable organic bases include salts of primary, secondary, and tertiary amines; substituted amines including naturally occurring substituted amines; and cyclic amines.

35 Particular pharmaceutically acceptable organic bases include arginine, betaine, caffeine, choline, N,N'-dibenzylethylenediamine, diethylamine, 2-diethylaminoethanol, 2-dimethylaminoethanol, ethanolamine, ethylenediamine, N-ethyl-morpholine, N-ethylpiperidine, glucamine, glucosamine, histidine, hydramine, isopropylamine, lysine, methylglucamine, morpholine, piperazine, piperidine, procaine, purines, theobromine, triethylamine,

40 trimethylamine, tripropyl amine, tromethamine, and the like. Salts may also be formed from basic ion exchange resins, for example polyamine resins. When the compound of the present invention is basic, salts may be prepared from pharmaceutically acceptable acids, including inorganic and organic acids. Such acids include acetic, benzenesulfonic, benzoic,

camphorsulfonic, citric, ethanesulfonic, ethanedisulfonic, fumaric, gluconic, glutamic, hydrobromic, hydrochloric, isethionic, lactic, maleic, malic, mandelic, methanesulfonic, mucic, pamoic, pantothenic, phosphoric, propionic, succinic, sulfuric, tartaric, p-toluenesulfonic acid, and the like.

5

The compounds of formula (I) may be prepared in crystalline or non-crystalline form, and if crystalline, may be optionally hydrated or solvated. This invention includes in its scope stoichiometric hydrates as well as compounds containing variable amounts of water.

10 Suitable solvates include pharmaceutically acceptable solvates, such as hydrates.

Solvates include stoichiometric solvates and non-stoichiometric solvates.

The terms "halogen" or "halo" are used to represent fluorine, chlorine, bromine or iodine.

15

The term "alkyl" as a group or part of a group means a straight, branched or cyclic chain alkyl group or combinations thereof. Unless hereinbefore defined, examples of alkyl include C₁₋₆alkyl, for example methyl, ethyl, n-propyl, iso-propyl, n-butyl, sec-butyl, iso-butyl, t-butyl, pentyl, hexyl, 1,1-dimethylethyl, cyclopentyl or cyclohexyl or combinations thereof such as cyclohexylmethyl and cyclopentylmethyl.

20

The term "alkoxy" as a group or as part of a group means a straight, branched or cyclic chain alkoxy group. Unless hereinbefore defined "alkoxy" includes C₁₋₆alkoxy, e.g. methoxy, ethoxy, n-propoxy, iso-propoxy, n-butoxy, sec-butoxy, iso-butoxy, tert-butoxy, pentoxy, hexyloxy, cyclopentoxy or cyclohexyloxy. In one aspect "alkoxy" is C₁₋₆ alkoxy.

25

The term "alkenyl" means linear or branched structures and combinations thereof, of the indicated number of carbon atoms, having at least one carbon-to-carbon double bond, wherein hydrogen may be replaced by an additional carbon to carbon double bond. In one aspect "alkenyl" is C₂₋₆alkenyl, for example ethenyl, propenyl, 1-methylethenyl, butenyl and the like.

30

The term "alkynyl" means linear or branched structures and combinations thereof, of the indicated number of carbon atoms, having at least one carbon-to-carbon triple bond. C₂₋₆alkynyl, for example, includes ethynyl, propynyl, butynyl and the like.

35

The term "heterocyclyl" as a group or as part of a group means an aromatic or non-aromatic five or six membered ring which contains from 1 to 4 heteroatoms selected from nitrogen, oxygen or sulfur and is unsubstituted or substituted by, for example, up to three substituents. Examples of 5-membered heterocyclyl groups include furyl, dioxalanyl, pyrrolyl, oxazolyl, thiazolyl, imidazolyl, oxadiazolyl, thiadiazolyl, triazolyl, triazinyl, isothiazolyl, isoxazolyl, thiophenyl, pyrazolyl or tetrazolyl. Examples of 6-membered heterocyclyl groups are pyridyl, pyridazinyl, pyrimidinyl, pyrazinyl, triazinyl or tetrazinyl.

The term "aryl" as a group or part of a group means a 5- or 6- membered aromatic ring, for example phenyl, or a 7 to 12 membered bicyclic ring system where at least one of the rings is aromatic, for example naphthyl. An aryl group may be optionally substituted by

5 one or more substituents, for example up to 4, 3 or 2 substituents. Preferably the aryl group is phenyl.

The term "heteroaryl" as a group or as part of a group means a monocyclic five or six membered aromatic ring, or a fused bicyclic aromatic ring system comprising two of such

10 monocyclic five or six membered aromatic rings. These heteroaryl rings contain one or more heteroatoms selected from nitrogen, oxygen or sulfur, where N-oxides, sulfur oxides and sulfur dioxides are permissible heteroatom substitutions. A heteroaryl group may be optionally substituted by one or more substituents, for example up to 3 or up to 2 substituents. Examples of "heteroaryl" used herein include furyl, thienyl, pyrrolyl, imidazolyl, pyrazolyl, triazolyl, tetrazolyl, thiazolyl, oxazolyl, isoxazolyl, oxadiazolyl, thiadiazolyl, isothiazolyl, pyridinyl, pyrimidinyl, quinolinyl, isoquinolinyl, benzofuryl, benzothienyl, indolyl, and indazolyl.

20 The term "bicyclic heterocyclyl" when used herein means a fused bicyclic aromatic or non-aromatic bicyclic heterocyclyl ring system comprising up to four, preferably one or two, heteroatoms each selected from oxygen, nitrogen and sulphur. Each ring may have from 4 to 7, preferably 5 or 6, ring atoms. A bicyclic heteroaromatic ring system may include a carbocyclic ring. Examples of bicyclic heterocyclyl groups include quinolinyl, isoquinolinyl, quinoxalinyl, quinazolinyl, pyridopyrazinyl, benzoxazolyl, benzothiophenyl, benzimidazolyl, benzothiazolyl, benzoxadiazolyl, benzthiadiazolyl, indolyl, benztriazolyl or naphthyridinyl.

25 When the heteroatom nitrogen replaces a carbon atom in an alkyl group, or when nitrogen is present in a heteroaryl, heterocyclyl or bicyclic heterocyclyl group, the nitrogen atom will, where appropriate, be substituted by one or two substituents selected from hydrogen and C₁₋₆alkyl, preferably hydrogen and C₁₋₆alkyl, more preferably hydrogen.

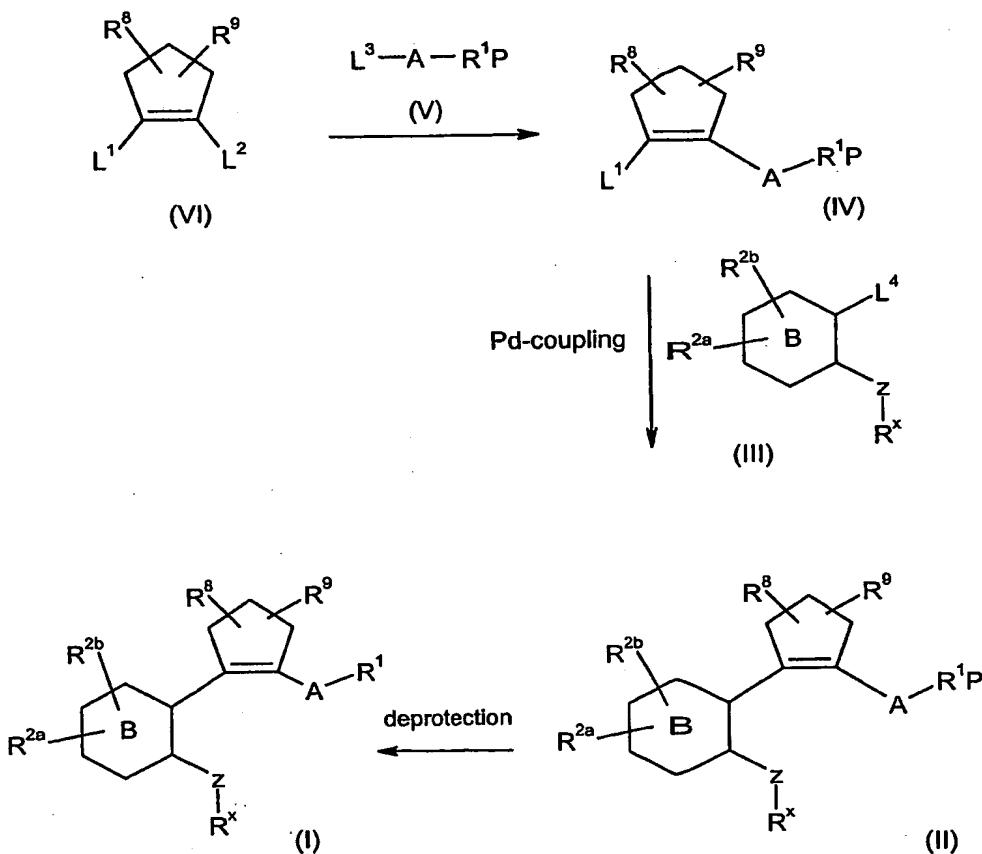
30 Optional substituents for alkyl or alkenyl groups unless hereinbefore defined include phenyl or halo e.g. Cl, Br or F. An alkyl or alkenyl group may be substituted by one or more optional substituents, for example up to 5, 4, 3, or 2 optional substituents. Particular substituted alkyl groups include those substituted by one or more fluorines e.g. CH₂F, CHF₂, CF₃, C₂F₅ etc, especially CF₃.

35 Optional substituents for alkoxy groups unless hereinbefore defined include halo e.g. Cl, Br or F. An alkoxy group may be substituted by one or more optional substituents, for example up to 5, 4, 3, or 2 optional substituents. Particular substituted alkoxy groups include those substituted by one or more fluorines e.g. OCH₂F, OCHF₂, OCF₃, OC₂F₅ etc.

Unless otherwise defined, optional substituents for aryl, heteroaryl or heterocyclyl moieties as a group or part of a group are selected from C₁₋₆alkyl, C₁₋₆alkoxy and halogen.

5 Compounds of formula (I) can be prepared as set forth in the following schemes and in the examples. The following processes form another aspect of the present invention.

For example, compounds of formula (I) may be prepared by the general route below:



10 wherein L¹ and L² each represent a leaving group for example halo, or triflate; L³ and L⁴ each represent an activating group, for example boronic acid; P is an optional protecting group; and A, B, R¹, R^{2a}, R^{2b}, R⁸, R⁹, Z and R^x are as defined for compounds of formula (I). L¹ can be converted to L^{1a}, and L² can be converted to L^{2a} wherein L^{1a} and L^{2a} each represent an activating group for example a boronic acid, and in this situation L³ and L⁴ can be halo or triflate.

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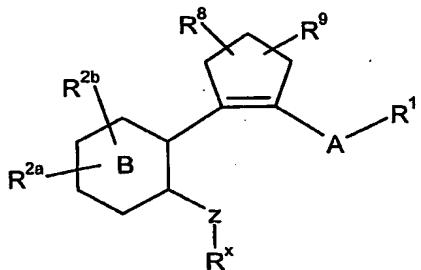
When R¹ is CO₂H examples of P include methyl, ethyl or optionally substituted benzyl esters.

20 Suitable reaction conditions for the deprotection of a compound of formula (II) include heating in aqueous ethanolic sodium hydroxide solution.

Suitable reaction conditions for the reaction of a compound of formula (VI) with a boronic acid of formula (V) (wherein L³ is -B(OH)₂) or a compound of formula (IV) with a boronic acid of formula (III) (wherein L⁴ is -B(OH)₂) include heating with

5 tetrakis(triphenylphosphine)palladium (0) and an inorganic base, for example potassium carbonate, in a solvent, e.g. ethylene glycol dimethyl ether (DME), toluene and ethanol, preferably in a ratio of 1:1.

Accordingly the present invention also provides a process for the preparation of a
10 compound of formula (I) or a derivative thereof:



(I)

wherein:

A represents an optionally substituted aryl, or an optionally substituted 5- or 6- membered heterocycl ring, or an optionally substituted bicyclic heterocycl group;
15 B represents a phenyl or pyridyl ring;
Z represents O, S, SO, or SO₂;
R¹ represents CO₂H, CN, CONR⁵R⁶, CH₂CO₂H, optionally substituted SO₂alkyl, SO₂NR⁵R⁶, NR⁵CONR⁵R⁶, COalkyl, 2H-tetrazol-5-yl-methyl, optionally substituted bicyclic heterocycle or optionally substituted heterocycl;
20 R^{2a} and R^{2b} each independently represents hydrogen, halo, optionally substituted alkyl, optionally substituted alkoxy, CN, SO₂alkyl, SR⁵, NO₂, optionally substituted aryl, CONR⁵R⁶ or optionally substituted heteroaryl;
R^x represents optionally substituted alkyl wherein 1 or 2 of the non-terminal carbon atoms
25 are optionally substituted by a group independently selected from NR⁴, O and SO_n, wherein n is 0, 1 or 2; optionally substituted alkenyl; or optionally substituted alkynyl; or R^x represents optionally substituted alkenyl, optionally substituted CQ^aQ^b-heterocycl, optionally substituted CQ^aQ^b-bicyclic heterocycl or optionally substituted CQ^aQ^b-aryl;
R⁴ represents hydrogen or an optionally substituted alkyl;
30 R⁵ represents hydrogen or an optionally substituted alkyl;
R⁶ represents hydrogen or optionally substituted alkyl, optionally substituted heteroaryl, optionally substituted SO₂aryl, optionally substituted SO₂alkyl, optionally substituted SO₂heteroaryl, CN, optionally substituted CQ^aQ^baryl, optionally substituted CQ^aQ^bheteroaryl or COR⁷;

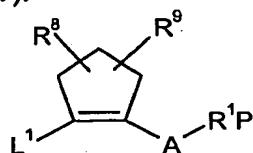
R⁷ represents hydrogen, optionally substituted alkyl, optionally substituted heteroaryl or optionally substituted aryl;

R⁸ and R⁹ each independently represents hydrogen, chloro, fluoro, CF₃, C₁₋₃alkoxy or C₁₋₃alkyl;

5 Q^a and Q^b are each independently selected from hydrogen and CH₃; wherein when A is a 6-membered ring the R¹ substituent and cyclopentene ring are attached to carbon atoms 1,2-, 1,3- or 1,4- relative to each other, and when A is a five-membered ring or bicyclic heterocycll group the R¹ substituent and cyclopentene ring are attached to substitutable carbon atoms 1,2- or 1,3- relative to each other;

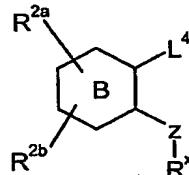
10 comprising:

reacting a compound of formula (IV):



(IV)

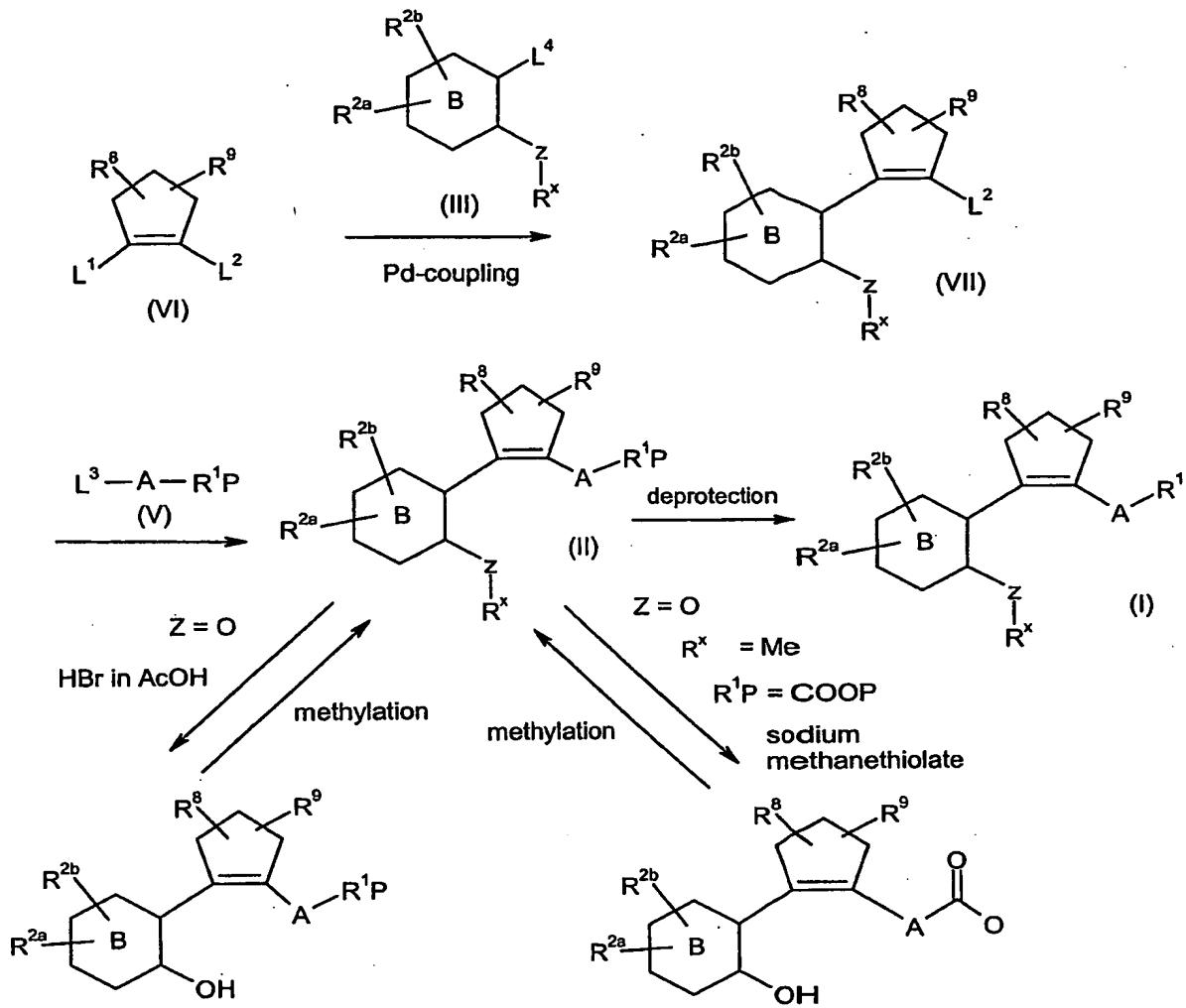
wherein R⁸, R⁹, A, and R¹ are as hereinbefore defined above for a compound of formula (I),
15 L¹ is a leaving group and P is an optional protecting group;
with a compound of formula (III):



(III)

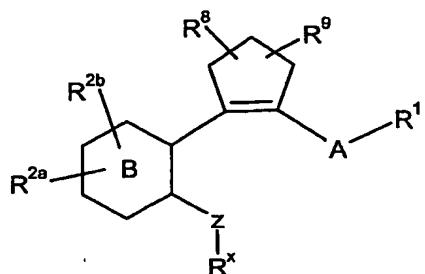
wherein R^{2a}, R^{2b}, B, Z, and R^x are as hereinbefore defined above for a compound of formula (I) and L⁴ is an activating group;
20 and where required converting:
one group A to another group A, and/or
one group R^x to another group R^x;
and where required carrying out the following optional steps in any order:
25 effecting deprotection; and/or
converting one group R¹ to another group R¹; and/or
forming a derivative of the compound of formula (I) so formed.

Alternatively compounds of formula (I) may be prepared according to the route described
30 below:



wherein L^1 , L^2 , L^3 , L^4 and P are as defined above, and A, B, R^1 , R^{2a} , R^{2b} , R^8 , R^9 , Z, and R^x are as defined for compounds of formula (I). L^1 can be converted to L^{1a} , and L^2 can be converted to L^{2a} wherein L^{1a} and L^{2a} each represent an activating group for example a boronic acid, and in this situation L^3 and L^4 can represent halo or triflate.

Accordingly the present invention also provides a process for the preparation of a compound of formula (I) or a derivative thereof:



(I)

wherein:

A represents an optionally substituted aryl, or an optionally substituted 5- or 6- membered heterocycl ring, or an optionally substituted bicyclic heterocycl group;

5 B represents a phenyl or pyridyl ring;

Z represents O, S, SO, or SO₂;

R¹ represents CO₂H, CN, CONR⁵R⁶, CH₂CO₂H, optionally substituted SO₂alkyl, SO₂NR⁵R⁶, NR⁵CONR⁵R⁶, COalkyl, 2H-tetrazol-5-yl-methyl, optionally substituted bicyclic heterocycle or optionally substituted heterocycl;

10 R^{2a} and R^{2b} each independently represents hydrogen, halo, optionally substituted alkyl, optionally substituted alkoxy, CN, SO₂alkyl, SR⁵, NO₂, optionally substituted aryl, CONR⁵R⁶ or optionally substituted heteroaryl;

R^x represents optionally substituted alkyl wherein 1 or 2 of the non-terminal carbon atoms are optionally substituted by a group independently selected from NR⁴, O and SO_n,

15 wherein n is 0, 1 or 2; optionally substituted alkenyl; or optionally substituted alkynyl; or R^x represents optionally substituted alkenyl, optionally substituted CQ^aQ^b-heterocycl, optionally substituted CQ^aQ^b-bicyclic heterocycl or optionally substituted CQ^aQ^b-aryl;

R⁴ represents hydrogen or an optionally substituted alkyl;

R⁵ represents hydrogen or an optionally substituted alkyl;

20 R⁶ represents hydrogen or optionally substituted alkyl, optionally substituted heteroaryl, optionally substituted SO₂aryl, optionally substituted SO₂alkyl, optionally substituted SO₂heteroaryl, CN, optionally substituted CQ^aQ^baryl, optionally substituted CQ^aQ^bheteroaryl or COR⁷;

R⁷ represents hydrogen, optionally substituted alkyl, optionally substituted heteroaryl or 25 optionally substituted aryl;

R⁸ and R⁹ each independently represents hydrogen, chloro, fluoro, CF₃, C₁₋₃alkoxy or C₁₋₃alkyl;

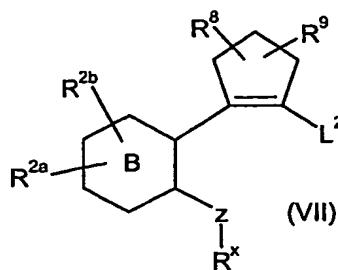
Q^a and Q^b are each independently selected from hydrogen and CH₃;

wherein when A is a 6-membered ring the R¹ substituent and cyclopentene ring are

30 attached to carbon atoms 1,2-, 1,3- or 1,4- relative to each other, and when A is a five-membered ring or bicyclic heterocycl group the R¹ substituent and cyclopentene ring are attached to substitutable carbon atoms 1,2- or 1,3- relative to each other;

comprising:

reacting a compound of formula (VII):



wherein R^{2a}, R^{2b}, R⁸, R⁹, A, B, R^x and R¹ are as hereinbefore defined above for a compound of formula (I), and L² is a leaving group;

5 with a compound of formula (V):



(V)

wherein R¹, and A are as hereinbefore defined above for a compound of formula (I); L³ is an activating group and P is an optional protecting group; and where required converting:

10 one group A to another group A, and/or

one group R^x to another group R^x;

and where required carrying out the following optional steps in any order:

effecting deprotection; and/or

converting one group R¹ to another group R¹; and/or

15 forming a derivative of the compound of formula (I) so formed.

It will be appreciated that certain substituents in intermediates and compounds of formula (I) may be converted to other substituents by conventional methods known to those skilled in the art.

20

A group R¹ may be converted to another group R¹ by use of conventional organic transformations known to those skilled in the art. For example R¹ = CO₂H may be converted to an amide, e.g. CONHCQ^aQ^baryl or CONHCQ^aQ^bheteroaryl wherein Q^a and Q^b are selected from hydrogen and CH₃, by conventional methods for the preparation of amides as described in, for example, Richard Larock, *Comprehensive Organic Transformations*, 2nd edition, Wiley-VCH, ISBN 0-471-19031-4.

25

Cyclopentene derivatives of formula (VI), boronic acids of formula (III) and (V), and tetrakis(triphenylphosphine)palladium (0) are commercially available, or readily prepared by methods known to those skilled in the art.

30

The preparation and reactions of boronic acids of formula (III) and formula (V) is reviewed in Suzuki *et al*, *Synth. Commun.*, 1981, 11, 513; Martin *et al*, *Acta. Chim. Scand.*, 1993, 47, 221; and Miyaura *et al*, *Chem. Rev.*, 1995, 95, 2457. For example, 2-benzyloxy-5-chlorophenylboronic acid may be prepared from 2-benzyloxy-5-chloro-iodobenzene. 2-

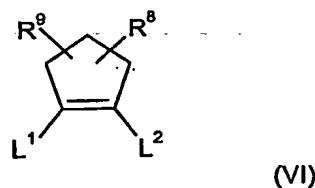
Benzylxy-5-chloro-iodobenzene may be prepared from 4-chloro-2-idoanisole by demethylation followed by benzylation according to known methods.

Certain substituents in any of the reaction intermediates and compounds of formula (I) 5 may be converted to other substituents by conventional methods known to those skilled in the art. Examples of substituents which may be converted include one group R^x to another group R^y ; and one substituent on a group A to another substituent on a group A. Examples of such transformations include the reduction of a nitro group to give an amino 10 group; alkylation and amidation of amino groups; hydrolysis of esters, alkylation of hydroxy and amino groups; and amidation and esterification of carboxylic acids. Such 15 transformations are well known to those skilled in the art and are described in for example, Richard Larock, *Comprehensive Organic Transformations*, 2nd edition, Wiley-VCH, ISBN, 0-471-19031-4.

15 For example, when R^x is p-methoxybenzyl, cleavage of the ether to give the phenol or pyridinol is carried out using, for example, using acid e.g. HCl/dioxane or using sodium methanethiolate. When R^x is methyl, cleavage of the ether to give the phenol is carried 20 out using, for example, sodium methanethiolate. Cleavage of the ether to give a pyridinol is carried out in the presence of, for example, trifluoroacetic acid. Conversion to another R^x group, for example a substituted benzyl group, may be effected by reaction of the 25 phenol or pyridinol with a suitable substituted benzyl bromide. The skilled person will appreciate that conversion of the protecting group P to another protecting group P may also occur under the reaction conditions used. When R^x is benzyl, cleavage of the ether to give the phenol or pyridinol may be carried out by hydrogenation according to known methods e.g. H_2 -Pd/C or NH_4CO_2H -Pd/C. The resulting phenol or pyridinol can then be converted to another group R^x as described above.

It will be appreciated by those skilled in the art that it may be necessary to protect certain reactive substituents during some of the above procedures. The skilled person will 30 recognise when a protecting group is required. Standard protection and deprotection techniques, such as those described in Greene T.W. 'Protective groups in organic synthesis', New York, Wiley (1981), can be used. For example, carboxylic acid groups can be protected as esters. Deprotection of such groups is achieved using conventional 35 procedures known in the art. It will be appreciated that protecting groups may be interconverted by conventional means.

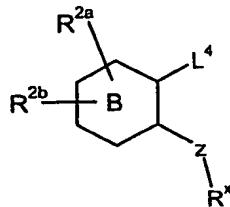
Cyclopentene intermediates of the formula (VI):



wherein L¹, L² are as defined above, and R⁸ and R⁹ are as hereinbefore defined for compounds of formula (I) are commercially available or may be readily prepared according to known methods.

5

Compounds of the formula (III):



10 wherein L⁴ is as hereinbefore defined, R^{2a}, R^{2b}, Z, B and R^x and are as defined for compounds of formula (I) are commercially available, or may readily be prepared by methods known to those skilled in the art, for example from suitable commercially available pyridinols, anisoles or phenols using methods as described in the examples.

15

Compounds of the formula (V):



20 wherein L³ and P are as defined above and R¹ and A are as hereinbefore defined for compounds of formula (I) are commercially available or may readily be prepared, for example, from suitable halobenzoic acid esters according to known methods, for example using methods as described in the examples.

25 It is to be understood that the present invention encompasses all isomers of formula (I) and their pharmaceutically acceptable derivatives, including all geometric, tautomeric and optical forms, and mixtures thereof (e.g. racemic mixtures). Where additional chiral centres are present in compounds of formula (I), the present invention includes within its scope all possible diastereoisomers, including mixtures thereof. The different isomeric forms may be separated or resolved one from the other by conventional methods, or any given isomer 30 may be obtained by conventional synthetic methods or by stereospecific or asymmetric syntheses.

The compounds of the invention bind to the EP₁ receptor and they are therefore considered to be useful in treating conditions mediated by the action of PGE₂ at EP₁ receptors.

35

Conditions mediated by the action of PGE₂ at EP₁ receptors include pain; fever; inflammation; immunological diseases; abnormal platelet function diseases; impotence or erectile dysfunction; bone disease; hemodynamic side effects of non-steroidal anti-

inflammatory drugs; cardiovascular diseases; neurodegenerative diseases and neurodegeneration; neurodegeneration following trauma; tinnitus; dependence on a dependence-inducing agent; complications of Type I diabetes; and kidney dysfunction.

5 The compounds of formula (I) are considered to be useful as analgesics. They are therefore considered useful in the treatment or prevention of pain.

10 The compounds of formula (I) are considered useful as analgesics to treat acute pain, chronic pain, neuropathic pain, inflammatory pain, visceral pain, pain associated with cancer and fibromyalgia, pain associated with migraine, tension headache and cluster headaches, and pain associated with functional bowel disorders, non-cardiac chest pain and non-ulcer dispepsia.

15 The compounds of formula (I) are considered useful in the treatment of chronic articular pain (e.g. rheumatoid arthritis, osteoarthritis, rheumatoid spondylitis, gouty arthritis and juvenile arthritis) including the property of disease modification and joint structure preservation; musculoskeletal pain; lower back and neck pain; sprains and strains; neuropathic pain; sympathetically maintained pain; myositis; pain associated with cancer and fibromyalgia; pain associated with migraine; pain associated with influenza or other

20 viral infections, such as the common cold; rheumatic fever; pain associated with functional bowel disorders such as non-ulcer dyspepsia, non-cardiac chest pain and irritable bowel syndrome; pain associated with myocardial ischemia; post operative pain; headache; toothache; and dysmenorrhea. The compounds of this invention may also be useful in the treatment of visceral pain.

25 The compounds of the invention are considered to be particularly useful in the treatment of neuropathic pain. Neuropathic pain syndromes can develop following neuronal injury and the resulting pain may persist for months or years, even after the original injury has healed. Neuronal injury may occur in the peripheral nerves, dorsal roots, spinal cord or certain regions in the brain. Neuropathic pain syndromes are traditionally classified according to the disease or event that precipitated them. Neuropathic pain syndromes include: diabetic neuropathy; sciatica; non-specific lower back pain; multiple sclerosis pain; fibromyalgia; HIV-related neuropathy; post-herpetic neuralgia; trigeminal neuralgia; and pain resulting from physical trauma, amputation, cancer, toxins or chronic inflammatory conditions. These conditions are difficult to treat and although several drugs are known to have limited efficacy, complete pain control is rarely achieved. The symptoms of neuropathic pain are heterogeneous and are often described as spontaneous shooting and lancinating pain, or ongoing, burning pain. In addition, there is pain associated with normally non-painful sensations such as "pins and needles" (paraesthesia and dysesthesias), increased sensitivity to touch (hyperesthesia), painful sensation following innocuous stimulation (dynamic, static or thermal allodynia), increased sensitivity to noxious stimuli (thermal, cold, mechanical hyperalgesia), continuing pain sensation after

It is to be understood that reference to treatment includes both treatment of established symptoms and prophylactic treatment, unless explicitly stated otherwise.

5 According to a further aspect of the invention, we provide a compound of formula (I) or a pharmaceutically acceptable derivative thereof for use in human or veterinary medicine.

10 According to another aspect of the invention, we provide a compound of formula (I) or a pharmaceutically acceptable derivative thereof for use in the treatment of a condition which is mediated by the action of PGE₂ at EP₁ receptors.

15 According to a further aspect of the invention, we provide a method of treating a human or animal subject suffering from a condition which is mediated by the action of PGE₂ at EP₁ receptors which comprises administering to said subject an effective amount of a compound of formula (I) or a pharmaceutically acceptable derivative thereof.

20 According to a further aspect of the invention we provide a method of treating a human or animal subject suffering from a pain, or an inflammatory, immunological, bone, neurodegenerative or renal disorder, which method comprises administering to said subject an effective amount of a compound of formula (I) or a pharmaceutically acceptable derivative thereof.

25 According to a yet further aspect of the invention we provide a method of treating a human or animal subject suffering from inflammatory pain, neuropathic pain or visceral pain which method comprises administering to said subject an effective amount of a compound of formula (I) or a pharmaceutically acceptable derivative thereof.

30 According to another aspect of the invention, we provide the use of a compound of formula (I) or a pharmaceutically acceptable derivative thereof for the manufacture of a medicament for the treatment of a condition which is mediated by the action of PGE₂ at EP₁ receptors.

35 According to another aspect of the invention we provide the use of a compound of formula (I) or a pharmaceutically acceptable derivative thereof for the manufacture of a medicament for the treatment or prevention of a condition such as a pain, or an inflammatory, immunological, bone, neurodegenerative or renal disorder.

40 According to another aspect of the invention we provide the use of a compound of formula (I) or a pharmaceutically acceptable derivative thereof for the manufacture of a medicament for the treatment or prevention of a condition such as inflammatory pain, neuropathic pain or visceral pain.

The compounds of formula (I) and their pharmaceutically acceptable derivatives are conveniently administered in the form of pharmaceutical compositions. Such compositions may conveniently be presented for use in conventional manner in admixture with one or more physiologically acceptable carriers or excipients.

5

Thus, in another aspect of the invention, we provide a pharmaceutical composition comprising a compound of formula (I) or a pharmaceutically acceptable derivative thereof adapted for use in human or veterinary medicine.

10 The compounds of formula (I) and their pharmaceutically acceptable derivatives may be formulated for administration in any suitable manner. They may be formulated for administration by inhalation or for oral, topical, transdermal or parenteral administration. The pharmaceutical composition may be in a form such that it can effect controlled release of the compounds of formula (I) and their pharmaceutically acceptable derivatives.

15

For oral administration, the pharmaceutical composition may take the form of, for example, tablets (including sub-lingual tablets), capsules, powders, solutions, syrups or suspensions prepared by conventional means with acceptable excipients.

20 For transdermal administration, the pharmaceutical composition may be given in the form of a transdermal patch, such as a transdermal iontophoretic patch.

For parenteral administration, the pharmaceutical composition may be given as an injection or a continuous infusion (e.g. intravenously, intravascularly or subcutaneously).

25 The compositions may take such forms as suspensions, solutions or emulsions in oily or aqueous vehicles and may contain formulatory agents such as suspending, stabilising and/or dispersing agents. For administration by injection these may take the form of a unit dose presentation or as a multidose presentation preferably with an added preservative. Alternatively for parenteral administration the active ingredient may be in powder form for 30 reconstitution with a suitable vehicle.

The compounds of the invention may also be formulated as a depot preparation. Such long acting formulations may be administered by implantation (for example subcutaneously or intramuscularly) or by intramuscular injection. Thus, for example, the compounds of the invention may be formulated with suitable polymeric or hydrophobic materials (for example as an emulsion in an acceptable oil) or ion exchange resins, or as sparingly soluble derivatives, for example, as a sparingly soluble salt.

40 The EP₁ receptor compounds for use in the instant invention may be used in combination with other therapeutic agents, for example COX-2 inhibitors, such as celecoxib, deracoxib, rofecoxib, valdecoxib, parecoxib or COX-189; 5-lipoxygenase inhibitors; NSAID's, such as diclofenac, indomethacin, nabumetone or ibuprofen; leukotriene receptor antagonists;

removal of the stimulation (hyperpathia) or an absence of or deficit in selective sensory pathways (hypoalgesia).

The compounds of formula (I) are also considered useful in the treatment of fever.

5

The compounds of formula (I) are also considered useful in the treatment of inflammation, for example in the treatment of skin conditions (e.g. sunburn, burns, eczema, dermatitis, psoriasis); ophthalmic diseases such as glaucoma, retinitis, retinopathies, uveitis and of acute injury to the eye tissue (e.g. conjunctivitis); lung disorders (e.g. asthma, bronchitis,

10

emphysema, allergic rhinitis, respiratory distress syndrome, pigeon fancier's disease, farmer's lung, chronic obstructive pulmonary disease, (COPD); gastrointestinal tract disorders (e.g. aphthous ulcer, Crohn's disease, atopic gastritis, gastritis varialoforme, ulcerative colitis, coeliac disease, regional ileitis, irritable bowel syndrome, inflammatory bowel disease, gastrointestinal reflux disease); organ transplantation; other conditions with

15

an inflammatory component such as vascular disease, migraine, periarthritis nodosa, thyroiditis, aplastic anaemia, Hodgkin's disease, sclerodoma, myasthenia gravis, multiple sclerosis, sarcoidosis, nephrotic syndrome, Bechet's syndrome, gingivitis, myocardial ischemia, pyrexia, systemic lupus erythematosus, polymyositis, tendinitis, bursitis, and Sjogren's syndrome.

20

The compounds of formula (I) are also considered useful in the treatment of immunological diseases such as autoimmune diseases, immunological deficiency diseases or organ transplantation. The compounds of formula (I) are also effective in increasing the latency of HIV infection.

25

The compounds of formula (I) are also considered useful in the treatment of diseases relating to abnormal platelet function (e.g. occlusive vascular diseases).

30

The compounds of formula (I) are also considered useful for the preparation of a drug with diuretic action.

The compounds of formula (I) are also considered useful in the treatment of impotence or erectile dysfunction.

35

The compounds of formula (I) are also considered useful in the treatment of bone disease characterised by abnormal bone metabolism or resorption such as osteoporosis (especially postmenopausal osteoporosis), hypercalcemia, hyperparathyroidism, Paget's bone disease, osteolysis, hypercalcemia of malignancy with or without bone metastases, rheumatoid arthritis, periodontitis, osteoarthritis, ostealgia, osteopenia, cancer cachexia, 40 calculosis, lithiasis (especially urolithiasis), solid carcinoma, gout and ankylosing spondylitis, tendinitis and bursitis.

The compounds of formula (I) are also considered useful for attenuating the hemodynamic side effects of non-steroidal anti-inflammatory drugs (NSAID's) and cyclooxygenase-2 (COX-2) inhibitors.

- 5 The compounds of formula (I) are also considered useful in the treatment of cardiovascular diseases such as hypertension or myocardial ischemia; functional or organic venous insufficiency; varicose therapy; haemorrhoids; and shock states associated with a marked drop in arterial pressure (e.g. septic shock).
- 10 The compounds of formula (I) are also considered useful in the treatment of neurodegenerative diseases and neurodegeneration such as dementia, particularly degenerative dementia (including senile dementia, Alzheimer's disease, Pick's disease, Huntingdon's chorea, Parkinson's disease and Creutzfeldt-Jakob disease, ALS, motor neuron disease); vascular dementia (including multi-infarct dementia); as well as dementia associated with intracranial space occupying lesions; trauma; infections and related conditions (including HIV infection); metabolism; toxins; anoxia and vitamin deficiency; and mild cognitive impairment associated with ageing, particularly Age Associated Memory Impairment.
- 15 The compounds of formula (I) are also considered useful in the treatment of neuroprotection and in the treatment of neurodegeneration following trauma such as stroke, cardiac arrest, pulmonary bypass, traumatic brain injury, spinal cord injury or the like.
- 20 The compounds of formula (I) are also considered useful in the treatment of tinnitus.
- 25 The compounds of formula (I) are also considered useful in preventing or reducing dependence on, or preventing or reducing tolerance or reverse tolerance to, a dependence inducing agent. Examples of dependence inducing agents include opioids (e.g. morphine), CNS depressants (e.g. ethanol), psychostimulants (e.g. cocaine) and nicotine.
- 30 The compounds of formula (I) are also considered useful in the treatment of complications of Type 1 diabetes (e.g. diabetic microangiopathy, diabetic retinopathy, diabetic nephropathy, macular degeneration, glaucoma), nephrotic syndrome, aplastic anaemia, uveitis, Kawasaki disease and sarcoidosis.
- 35 The compounds of formula (I) are also considered useful in the treatment of kidney dysfunction (nephritis, particularly mesangial proliferative glomerulonephritis, nephritic syndrome), liver dysfunction (hepatitis, cirrhosis), gastrointestinal dysfunction (diarrhoea) and colon cancer.
- 40 The compounds of formula (I) and pharmaceutically acceptable derivatives thereof are also useful in the treatment of overactive bladder and urge incontinence.

DMARD's such as methotrexate; adenosine A1 receptor agonists; sodium channel blockers, such as lamotrigine; NMDA receptor modulators, such as glycine receptor antagonists; gabapentin and related compounds; tricyclic antidepressants such as amitriptyline; neurone stabilising antiepileptic drugs; mono-aminergic uptake inhibitors

5 such as venlafaxine; opioid analgesics; local anaesthetics; 5HT₁ agonists, such as triptans, for example sumatriptan, naratriptan, zolmitriptan, eletriptan, frovatriptan, almotriptan or rizatriptan; nicotinic acetyl choline (nACh) receptor modulators; glutamate receptor modulators, for example modulators of the NR2B ssubtype; EP₄ receptor ligands; EP₂ receptor ligands; EP₃ receptor ligands; EP₄ antagonists; EP₂ antagonists and EP₃

10 antagonists; cannabinoid receptor ligands; bradykinin receptor ligands and vanilloid receptor ligand. When the compounds are used in combination with other therapeutic agents, the compounds may be administered either sequentially or simultaneously by any convenient route.

15 Additional COX-2 inhibitors are disclosed in US Patent Nos. 5,474,995 US5,633,272; US5,466,823, US6,310,099 and US6,291,523; and in WO 96/25405, WO 97/38986, WO 98/03484, WO 97/14691, WO99/12930, WO00/26216, WO00/52008, WO00/38311, WO01/58881 and WO02/18374.

20 The invention thus provides, in a further aspect, a combination comprising a compound of formula (I) or a pharmaceutically acceptable derivative thereof together with a further therapeutic agent or agents.

25 The combinations referred to above may conveniently be presented for use in the form of a pharmaceutical formulation and thus pharmaceutical formulations comprising a combination as defined above together with a pharmaceutically acceptable carrier or excipient comprise a further aspect of the invention. The individual components of such combinations may be administered either sequentially or simultaneously in separate or combined pharmaceutical formulations.

30 When a compound of formula (I) or a pharmaceutically acceptable derivative thereof is used in combination with a second therapeutic agent active against the same disease state the dose of each compound may differ from that when the compound is used alone. Appropriate doses will be readily appreciated by those skilled in the art.

35 A proposed daily dosage of compounds of formula (I) or their pharmaceutically acceptable derivatives for the treatment of man is from 0.01 to 30 mg/kg body weight per day and more particularly 0.1 to 10 mg/kg body weight per day, which may be administered as a single or divided dose, for example one to four times per day. The dose range for adult

40 human beings is generally from 8 to 2000 mg/day, such as from 20 to 1000 mg/day, preferably 35 to 200 mg/day.

The precise amount of the compounds of formula (I) administered to a host, particularly a human patient, will be the responsibility of the attendant physician. However, the dose employed will depend on a number of factors including the age and sex of the patient, the precise condition being treated and its severity, and the route of administration.

5

No unacceptable toxicological effects are expected with compounds of the invention when administered in accordance with the invention.

10 All publications, including but not limited to patents and patent applications, cited in this specification are herein incorporated by reference as if each individual publication were specifically and individually indicated to be incorporated by reference herein as though fully set forth.

15 The following non-limiting Examples illustrate the preparation of pharmacologically active compounds of the invention.

EXAMPLES**ABBREVIATIONS**

5 Bn (benzyl), Bu, Pr, Me, Et (butyl, propyl, methyl ethyl), DMSO (dimethyl sulfoxide), DCM (dichloromethane), DME (ethylene glycol dimethyl ether), DMF (N,N-dimethylformamide), EDC (1-(3-dimethylaminopropyl)-3-ethylcarbodiimide), EDTA (ethylenediamine tetraacetic acid), EtOAc (ethyl acetate), EtOH (ethanol), HPLC (High pressure liquid chromatography), LCMS (Liquid chromatography/Mass spectroscopy), MDAP (Mass Directed Purification), MeCN (acetonitrile), MeOH (methanol), NMR (Nuclear Magnetic Resonance (spectrum)), Ph (phenyl), pTSA (para-toluene sulphonic acid), SPE (Solid Phase Extraction), TBAF (tetrabutylammonium fluoride), THF (tetrahydrofuran), s, d, t, q, m, br (singlet, doublet, triplet, quartet, multiplet, broad.)

10

15 LCMS

- Column: 3.3cm x 4.6mm ID, 3um ABZ+PLUS
- Flow Rate: 3ml/min
- Injection Volume: 5 μ l

20 • Temp: RT

- UV Detection Range: 215 to 330nm
-

Solvents: A: 0.1% Formic Acid + 10mMolar Ammonium Acetate.
 B: 95% Acetonitrile + 0.05% Formic Acid

Gradient:	Time	A%	B%
	0.00	100	0
	0.70	100	0
	4.20	0	100
	5.30	0	100
	5.50	100	0

25 MASS DIRECTED AUTOPREPARATION**Hardware:**

Waters 600 gradient pump
 Waters 2767 inject/collector
 Waters Reagent Manager
 Micromass ZMD mass spectrometer
 Gilson Aspec - waste collector
 Gilson 115 post-fraction UV detector

Software:

35 Micromass Masslynx version 4.0

Column

The column used is typically a Supelco LCABZ++ column whose dimensions are 20mm internal diameter by 100mm in length. The stationary phase particle size is 5 μ m.

Solvents:

5 A.: Aqueous solvent = Water + 0.1% Formic Acid
B: Organic solvent = MeCN: Water 95:5 +0.05% Formic Acid
Make up solvent = MeOH: Water 80:20 +50mMol Ammonium Acetate
Needle rinse solvent = MeOH: Water: DMSO 80:10:10

10 The method used depends on the analytical retention time of the compound of interest.
15-minute runtime, which comprises a 10-minute gradient followed by a 5-minute column flush and re-equilibration step.
MDP 1.5-2.2 = 0-30% B
MDP 2.0-2.8 = 5-30% B

15 MDP 2.5-3.0 = 15-55% B
MDP 2.8-4.0 = 30-80% B
MDP 3.8-5.5 = 50-90% B

Flow rate:
flow rate 20ml/min.

20

PREPARATION OF INTERMEDIATES

1-[(Phenylmethyl)oxy]-4-(trifluoromethyl)benzene

25 A solution of 4-(trifluoromethyl)phenol (8.55g, 52.78mmol) in acetone (200ml) was treated with benzyl bromide (9.87g, 6.86ml, 58.05mmol) and potassium carbonate (10.94g, 79.16mmol). The mixture was stirred and heated to reflux under nitrogen for 3h. After cooling, diethyl ether (400ml) and water (400ml) were added and the aqueous phase re-extracted with diethyl ether (100ml). The combined organic layers were washed with water, dried ($MgSO_4$) and the solvent removed *in vacuo* to leave the title compound as a white solid. (12.71g, 95%)
 1H NMR ($CDCl_3$) δ : 5.11 (2H,s), 7.03 (2H, d), 7.34-7.44 (5H, m), 7.55 (2H, d).

2-Iodo-1-[(phenylmethyl)oxy]-4-(trifluoromethyl)benzene

35

A solution of 1-[(phenylmethyl)oxy]-4-(trifluoromethyl)benzene (12.71g, 50.4mmol) in acetonitrile (300ml) was stirred under nitrogen and 1-(chloromethyl)-4-fluoro-1,4-diazoniabicyclo[2.2.2]octane bis(tetrafluoroborate) (17.75g, 50.4mmol) and iodine (6.4g, 25.2mmol) added. The mixture was stirred at room temperature for 88h. The solvent was evaporated and the residue partitioned between ethyl acetate (400ml) and water (400ml). The organic layer was washed with water, dried ($MgSO_4$) and evaporated to an orange oil

which was purified by flash chromatography (silica gel, 5% ethyl acetate: isohexane) to give the title compound as an orange oil (15.07g, 79%)

¹H NMR (CDCl₃) δ: 5.21 (2H, s), 6.89 (1H, d J), 7.32-7.55 (6H, m), 8.04 (1H, d).

5 1-Chloro-5-iodo-2-methyl-4-(methyloxy)benzene

A mixture of 1-chloro-5-iodo-2-methyl-4-(methyloxy)benzene (5.0g, 32 mmol), 1-(chloromethyl)-4-fluoro-1,4-diazoniabicyclo[2.2.2]octane bis(tetrafluoroborate) (11.3g, 32mmol), and iodine (4.06g, 16mmol) in dry acetonitrile (100ml) was stirred at room

10 temperature for 6 hours. The solvent was evaporated at < 30°C. The residue was partitioned between ethyl acetate (50ml) and water (50ml). The organic phase was dried (MgSO₄) and evaporated to leave the title compound as a yellow gum (9.0g).

¹H NMR (CDCl₃) δ: 2.31(3H,s), 3.83(3H,s), 6.65(1H, s), 7.68(1H, s).

15 4,5-dichloro-2-iodophenyl methyl ether

The title compound was prepared in a similar manner to 1-Chloro-5-iodo-2-methyl-4-(methyloxy)benzene using 4,5-dichlorophenyl methyl ether.

¹H NMR (CDCl₃) δ: 3.87(3H,s), 6.87(1H,s), 7.82(1H,s).

20

Ethyl 5-ido-2-methylbenzoate

A solution of 5-amino-2-methylbenzoic acid ethyl ester (500mg, 2.8mmol) and iodine (425mg, 1.68mmol) in toluene (20ml) was cooled to 0°C and treated with t-butyl nitrite

25 (303mg, 2.94mmol). The reaction mixture was stirred at 0°C for 1 hour then at room temperature for 72 hours. The reaction mixture was washed with 10% aqueous sodium thiosulphate (20ml),and brine (20ml), dried (MgSO₄) and evaporated. Flash chromatography [silica, iso-hexane/EtOAc, 9:1] gave ethyl 5-ido-2-methylbenzoate as a brown oil (510mg).

30 ¹H NMR (CDCl₃) δ: 1.39(3H, t), 2.53(3H, s), 4.36(2H, q), 6.97(1H, d), 7.37(1H, d), 8.20(1H, s).

Ethyl 2-fluoro-5-iodobenzoate

35 Ethyl 2-fluoro-5-aminobenzoate (6.5g, 35.48mmol) was stirred in 5N hydrochloric acid (60ml) and cooled to 0°C. Sodium nitrite (2.7g, 39.03mmol) in water (5ml) was added at 0-5°C. The resulting mixture was added to a solution of potassium iodide (7.07g, 42.58mmol) in water (50ml) over 5 minutes. The reaction was stirred at room temperature for 1 hour, then extracted with diethyl ether. The organic solution was washed with water

40 and 5% sodium thiosulphate solution, dried (MgSO₄) and evaporated. The residue was purified by flash chromatography, eluting with 5% ethyl acetate/isohexane to give the title compound as a colourless oil (7.8g).

¹H NMR (CDCl₃) δ: 1.40(3H, t), 4.39(2H, q), 6.91(1H, dd), 7.79(1H, td), 8.22(1H, dd).

Ethyl 3-fluoro-5-nitrobenzoate

5-Fluoro-3-nitrobenzoic acid (4.8g, 25.92mmol) was dissolved in ethanol (50ml) and
5 sulphuric acid (0.5ml) added carefully. The mixture was heated to reflux for 16 hours. The solvent was evaporated and the residue dissolved in ethyl acetate and washed with water, 5% sodium bicarbonate solution and brine, dried ($MgSO_4$) and evaporated. The residue was purified by flash chromatography, eluting with 10% ethyl acetate/isohexane to give the title compound as a yellow oil (2.04g)
10 1H NMR ($CDCl_3$) δ : 1.44(3H, t), 4.46(2H, q), 8.07-8.14(2H, m), 8.69(1H, s).

Ethyl 3-amino-5-fluorobenzoate

Ethyl 3-fluoro-5-nitrobenzoate (5.0g, 23.46mmol) was dissolved in ethanol (150ml) and
15 tin(II)chloride (44.24g, 0.234mol) added portionwise with stirring. The mixture was stirred at 80°C for 1 hour. The solvent was evaporated and the residue partitioned between ethyl acetate and 2M sodium hydroxide solution. The resulting glutinous mixture was slowly filtered through a Kieselguhr bed, which was washed copiously with ethyl acetate. The organic phase was washed with water, dried ($MgSO_4$) and evaporated to give the title
20 compound as a cream solid (3.98g).
 1H NMR ($CDCl_3$) δ : 1.38(3H, t), 3.94(2H, br s), 4.35(2H, q), 6.53(1H, dd), 7.08(1H, dd), 7.14(1H, d).

Ethyl 3-fluoro-5-iodobenzoate

25 Ethyl 3-fluoro-5-aminobenzoate (3.98g, 21.73mmol) was stirred in 5N hydrochloric acid (45ml) and cooled to 0°C. Sodium nitrite (1.65g, 23.91mmol) in water (2ml) was added at 0-5°C. The resulting mixture was added dropwise to a solution of potassium iodide (4.33g, 26.09mmol) in water (30ml) over 20 minutes. The reaction was stirred at room
30 temperature for 1 hour, then extracted with diethyl ether (x2). The organic solution was washed with water and 5% sodium thiosulphate solution, dried ($MgSO_4$) and evaporated to give the title compound as an orange oil (5.0g).
 1H NMR ($CDCl_3$) δ : 1.40(3H, t), 4.39(2H, q), 7.62(1H, dd), 7.69(1H, td), 8.17(1H, s).

35 Ethyl 3-amino-5-nitrobenzoate

3-Amino-5-nitrobenzoic acid (10.0g, 54.9mmol) was dissolved in ethanol (100ml) and treated with conc. sulphuric acid (5ml). The mixture was heated at reflux overnight. After cooling the ethanol was removed in vacuo and the residue was dissolved in diethyl ether.
40 The solution was basified with saturated aqueous sodium bicarbonate and the layers separated. The aqueous layer was further extracted with diethyl ether (x3) and the

combined organic extracts were dried (Na_2SO_4) and concentrated in vacuo to give the ester (6.5g).

^1H NMR (CDCl_3) δ : 1.41(3H, t), 4.15(2H, br s), 4.40(2H, q), 7.60-7.68(2H, m), 8.20(1H, s).

5 Ethyl 3-iodo-5-nitrobenzoate

Ethyl 3-amino-5-nitrobenzoate (6.5g, 30.9mmol) was suspended in 5M aqueous HCl (50ml), cooled to 0°C and sodium nitrite (2.34g, 33.9mmol) in water (4ml) was added slowly. The resulting solution of the diazonium salt was added slowly to a solution of 10 potassium iodide (6.16g, 37.1mmol) in water (40ml), and the resulting mixture was stirred at room temperature for 1 hour. The mixture was extracted with diethyl ether, and the extract was washed with water and aqueous sodium thiosulphate solution, dried (Na_2SO_4) and concentrated *in vacuo*. The residue was purified by flash chromatography on silica (gradient elution, 10-20% ethyl acetate/cyclohexane) to give the title compound (5.46g).

15 ^1H NMR (CDCl_3) δ : 1.44(3H, t), 4.46(2H, q), 8.68(1H, t), 8.73(1H, t), 8.81(1H, t).

Ethyl 3-amino-5-iodobenzoate

Ethyl 3-iodo-5-nitrobenzoate (4.45g, 13.9mmol) was dissolved in ethanol and tin (II)

20 chloride (27g, 146mmol) was added. The mixture was heated to reflux for 2 hours. After cooling, the reaction was concentrated *in vacuo*. The residue was partitioned between ethyl acetate and aqueous sodium hydroxide solution, and the aqueous extracted with further ethyl acetate. The combined extracts were washed with water, dried (Na_2SO_4) and concentrated in vacuo to give the title compound as a yellow oil which slowly crystallised 25 (3.56g). LC/MS Rt=3.23min [MH^+] 292.

^1H NMR (CDCl_3) δ : 1.38(3H, t), 3.80 (2H, br s), 4.45(2H, q), 7.20(1H, t), 7.30(1H, t), 7.74(1H, t).

3-Bromo-5-chloro-2(1H)-pyridinone

30 5-Chloro-2-pyridinol (5.18g, 40mmol) was dissolved in glacial acetic acid(50ml) and bromine (7.51g, 2.41ml, 47mmol) added dropwise. The mixture was stirred at room temperature for 48 hours. Ethyl acetate and water were added and the organic layer washed with water (x3), dried (MgSO_4) and evaporated. The residue was triturated with diethyl ether and the buff solid filtered and dried (5.59g).

^1H NMR (CDCl_3) δ : 7.52(1H, d), 7.87(1H, d).

3-Bromo-5-chloro-2-[(phenylmethyl)oxy]pyridine

40 3-Bromo-5-chloro-2-pyridinol (7.0g, 33.6mmol) was stirred in toluene (160ml) and silver carbonate (10.23g, 36.9mmol) added, followed by benzyl bromide (6.32g, 4.39ml, 36.9mmol). The mixture was heated to reflux for 1 hour. After cooling, the mixture was

filtered, washed with water (x2), dried ($MgSO_4$) and evaporated. The residue was triturated with isohexane and the pale yellow solid filtered and dried. (8.36g).

1H NMR ($CDCl_3$) δ : 5.43(2H, s), 7.32-7.48(5H, m), 7.82(1H, d), 8.04(1H, d).

5 5-Chloro-3-iodo-2-[(phenylmethyl)oxy]pyridine

5-Chloro-3-iodo-2(1*H*)-pyridinone (6.69g, 26.18mmol) was dissolved in toluene (125ml) and silver carbonate (7.97g, 28.8mmol) added, followed by benzyl bromide (3.43ml, 28.8mmol). The mixture was stirred and heated to reflux for 2 hours. The mixture was cooled, filtered through a Kieselguhr pad and the solvent evaporated. The residue was triturated with isohexane containing a trace of diethyl ether and the title compound filtered and dried *in vacuo* (6.8g).

1H NMR ($CDCl_3$) δ : 5.41(2H, s), 7.32-7.49(5H, m), 8.03(1H, d), 8.06(1H, d).

15 3-Iodo-2-[(phenylmethyl)oxy]-5-(trifluoromethyl)pyridine

The title compound was prepared in a similar manner to 5-chloro-3-iodo-2-[(phenylmethyl)oxy]pyridine using 3-iodo-5-(trifluoromethyl)-2(1*H*)-pyridinone.

1H NMR ($CDCl_3$) δ : 5.49(2H, s), 7.33-7.50(5H, m), 8.23(1H, d), 8.39(1H, d).

20 Ethyl 3-bromo-5-fluorobenzoate

3-Bromo-5-fluorobenzoic acid (ex. Fluorochem) (6.0g, 22.8mmol) was dissolved in ethanol (50ml) and treated with conc. sulphuric acid (2.5ml). The mixture was heated at reflux overnight. After cooling the ethanol was removed *in vacuo* and the residue was dissolved in diethyl ether. The solution was basified with saturated aqueous sodium bicarbonate, and the layers separated. The aqueous layer was further extracted with diethyl ether (x3), and the combined organic extracts were dried (Na_2SO_4) and concentrated *in vacuo* to give the ester (6.17g).

30 1H NMR ($CDCl_3$) δ : 1.41 (3H, t), 4.40 (2H, q), 7.44 (1H, dt), 7.68 (1H, ddd), 7.99(1H, s).

Ethyl 3-amino-5-nitrobenzoate

3-Amino-5-nitrobenzoic acid (ex Lancaster) (10.0g, 54.9mmol) was dissolved in ethanol (100ml) and treated with conc. sulphuric acid (5ml). The mixture was heated at reflux overnight. After cooling the ethanol was removed *in vacuo* and the residue was dissolved in diethyl ether. The solution was basified with saturated aqueous sodium bicarbonate, and the layers separated. The aqueous layer was further extracted with diethyl ether (x3), and the combined organic extracts were dried (Na_2SO_4) and concentrated *in vacuo* to give the ester (6.5g).

40 1H NMR ($CDCl_3$) δ : 1.41(3H, t), 4.15(2H, br s), 4.40(2H, q), 7.60-7.68(2H, m), 8.20(1H, s).

Ethyl 3-iodo-5-nitrobenzoate

Ethyl 3-amino-5-nitrobenzoate (6.5g, 30.9mmol) was suspended in 5M aqueous HCl (50ml), cooled to 0°C, and treated with aqueous sodium nitrite (2.34g 33.9mmol in 4ml water) added slowly. The resulting solution of the diazonium salt was added slowly to a
5 solution of potassium iodide (6.16g, 37.1mmol) in water (40ml), and the resulting mixture was stirred at room temperature for 1 hour. The mixture was extracted with diethyl ether, and the extract was washed with water, aqueous sodium thiosulphate solution, dried (Na₂SO₄) and concentrated *in vacuo*. The residue was purified by flash chromatography on silica (gradient elution, 10-20% ethyl acetate/cyclohexane) to give the title compound
10 (5.46g).

¹H NMR (CDCl₃) δ: 1.44(3H, t), 4.46(2H,q), 8.68(1H, t), 8.73(1H, t), 8.81(1H, t).

Ethyl 3-amino-5-iodobenzoate

15 Ethyl 3-iodo-5-nitrobenzoate (4.45g, 13.9mmol) was dissolved in ethanol and tin (II) chloride (27g, 146mmol) was added. The mixture was heated to reflux for 2 hours, by which time LC/MS analysis showed that reaction was complete. After cooling, the reaction was concentrated *in vacuo*. The residue was partitioned between ethyl acetate and aqueous sodium hydroxide solution, and the aqueous extract was further ethyl acetate.
20 The combined extracts were washed with water, dried (Na₂SO₄) and concentrated *in vacuo* to give the title compound as a yellow oil which slowly crystallised (3.56g).

¹H NMR (CDCl₃) δ: 1.38(3H, t), 3.80 (2H, br s), 4.45(2H, q), 7.20(1H, t), 7.30(1H, t), 7.74(1H, t). LC/MS Rt=3.23min [MH⁺] 292.

25 Ethyl 3,6-dichloro-2-pyridinecarboxylate

3,6-Dichloro-2-pyridinecarboxylic acid (530mg, 2.76mmol) was dissolved in a mixture of ethanol (20ml) and sulphuric acid (0.25ml) and refluxed for 2 hours then left at room temperature for 3 days. The resulting solution was evaporated and the residue dissolved in
30 diethyl ether/water and basified with potassium carbonate. The organic layer was dried (magnesium sulphate) and evaporated to give a colourless oil (602mg).
LC/MS t=2.56, [MH⁺] 220.3

Ethyl 3-methyl-2-pyridinecarboxylate 1-oxide

35 A solution of ethyl 3-methyl-2-pyridinecarboxylate (12.1g, 73mmol) and 3-chloroperbenzoic acid (28g, 50-55%, 80mmol) in dichloromethane (200ml) was left at room temperature for 16 hours then washed with sodium thiosulphate solution and sodium bicarbonate solution. The organic solution was dried (magnesium sulphate) and evaporated to give a light
40 coloured oil (12.2g). LC/MS Rt=1.39, [MH⁺] 182.3

Ethyl 6-chloro-3-methyl-2-pyridinecarboxylate

Ethyl 3-methyl-2-pyridinecarboxylate 1-oxide (12.1g, 66.85mmol) was added in portions with water bath cooling to phosphorus oxychloride (50ml) and the resulting mixture stirred for 30 minutes and evaporated to dryness. The residue was dissolved in diethyl ether/water and basified with 2M sodium hydroxide solution. The organic layer was

5 separated, dried (magnesium sulphate), evaporated and purified by chromatography on silica eluting with ethyl acetate/iso-hexane (1:9) to give a colourless oil (2.4g).
LC/MS Rt=2.52, [MH+] 200.3, 202.3
¹H NMR (CDCl₃) δ: 1.43 (3H, t), 2.54 (3H, s), 4.44 (2H, q), 7.35 (1H, d), 7.57 (1H, d).

10 Methyl 5-chloro-2-ethyl-3-pyridinecarboxylate

Potassium-tert-butoxide (1.176 g, 10.5 mmol) was added slowly to a stirring solution of methyl 3-oxopentanoate (1.30 g, 10 mmol) in tetrahydrofuran (33 ml) and stirred for 45 minutes before adding 2-chloro-1,3-bis(dimethylamino)trimethinium hexafluorophosphate (4.6 g, 15.00 mmol) and 1,4-diazabicyclo(2.2.2) octane (1.12 g, 10 mmol) and stirring at 45°C for 3 hours. Ammonium acetate (1.54 g, 20 mmols) was added and the reaction mixture was refluxed for 6 hours. The reaction mixture was cooled to room temperature and diluted with diethyl ether and water. The ether layer was separated, dried over magnesium sulphate and evaporated to dryness to give the title compound as a yellow oil.

20 1.24 g, 62%. LC/MS: Rt = 2.65 min, [M+H] 200.

Methyl 5-bromo-2-(trifluoromethyl)-3-pyridinecarboxylate

(Trimethylsilyl)diazomethane (2M solution in hexanes, 5ml, 10mmol) was added to a solution of 5-bromo-2-(trifluoromethyl)-3-pyridinecarboxylic acid (Eur. J. Org. Chem. 2002, 327-330) (2.05g, 7.59mmol) in tetrahydrofuran (10ml). The resulting solution was evaporated to dryness and the residue purified by chromatography on silica eluting with ethyl acetate/iso-hexane (1:19) to give 950mg of pale coloured oil.

¹H NMR (CDCl₃) δ: 3.84 (3H, s), 8.12 (1H, d), 8.71 (1H, d).

30 Ethyl 6-chloro-4-(trifluoromethyl)-2-pyridinecarboxylate

A mixture of 6-chloro-4-(trifluoromethyl)-2-pyridinecarboxylic acid (5g, 22.16mmol) sulphuric acid (5ml) and ethanol (80ml) was stirred and refluxed for 14 hours then cooled and evaporated. The residue was dissolved in ether/water and basified with aqueous ammonia. The organic layer was dried (magnesium sulphate) and evaporated to give the title compound as a colourless oil (4.88g).

LC/MS: [M+H] 254.3, 256.4, Rt=2.98min

40 (2-Bromo-1-cyclopenten-1-yl)boronic acid

1,2-Dibromocyclopentene (10.1 g, 0.044 mol) was dissolved in 100 mL of tetrahydrofuran , cooled to -78°C and n-butyllithium (1.6 M solution in hexanes; 28 mL, 0.044 mol), was

added dropwise over 20 minutes under nitrogen. The mixture was stirred at -78°C for 20 minutes, then triisopropylborate (20.8 mL, 0.089 mol) was added dropwise. The cooling bath was then removed and the reaction mixture was allowed to reach room temperature. The reaction mixture was then quenched with 1M HCl (40 mL) and stirred vigorously at 5 room temperature for 15 minutes. The organic layer was separated, dried over magnesium sulphate and evaporated down. The residue was triturated with dichloromethane to yield the title compound as a white solid (2.2g, 26%).
¹H NMR (CDCl₃) δ: 1.92-1.98 (2H, m), 2.50-2.55 (2H, m), 2.73-2.78(2H, m), 5.02 (2H, s).

10 [2-(Methyloxy)-5-(trifluoromethyl)phenyl]boronic acid

2-Bromo-1-methoxy-4-(trifluoromethyl)benzene (20g, 78mmol) was dissolved in dry Et₂O (300ml) and cooled to -70°C, n-butyllithium (1.6M solution in hexanes; 53.4ml, 86mmol) was added slowly keeping the temperature at about -70°C and the reaction stirred for 30 minutes. Tri-isopropyl borate (36.2ml, 0.16mol) was added slowly keeping the temperature at about -70°C and the reaction allowed to warm to RT and stirred under nitrogen for 16 hours. 2N HCl (300ml) was added and the reaction stirred vigorously for 3 hours. The reaction was diluted with EtOAc and the organics separated, the aqueous washed with 3 x EtOAc. The combined organics were then washed with brine, dried over 20 MgSO₄, filtered and concentrated in vacuo to yield a yellow oil, this was triturated in *iso*-hexane to yield a white solid (14.6g, 85%). LC/MS Rt = 2.57.

{5-Chloro-2-[(phenylmethyl)oxy]-3-pyridinyl}boronic acid

25 a) 3-Bromo-5-chloro-2-[(phenylmethyl)oxy]pyridine (3.65g, 12.21mmol) was dissolved in diethyl ether (80ml) and added dropwise to a stirring solution of 1.6M n-butyllithium in hexanes (9.16ml, 14.6mmol) in diethyl ether (20ml) at -78°C under nitrogen over 30 minutes. The mixture was stirred at -78°C for 1 hour. Triisopropyl borate (3.37ml, 14.6mmol) in diethyl ether (10ml) was added dropwise over 10 minutes at -78°C. The reaction was allowed to warm to room temperature then stirred for 1 hour. 2M sodium hydroxide solution (100ml) was added and the mixture stirred for 15 minutes. The layers were separated and the organic layer re-extracted with 2M sodium hydroxide solution (50ml). The combined aqueous layers were acidified to pH6 with 2M hydrochloric acid solution at <10°C and extracted with ethyl acetate (x2). The combined organic phases were washed with water, dried (MgSO₄) and evaporated to a white solid (1.83g).
¹H NMR (CDCl₃) δ: 5.45(2H, s), 5.71(2H, s), 7.36-7.45(5H, m), 8.09(1H, d), 8.20(1H, d).
b) 5-Chloro-3-iodo-2-[(phenylmethyl)oxy]pyridine (3.35g, 9.7mmol) was dissolved in tetrahydrofuran (50ml) under nitrogen and cooled to -40°C. 2M isopropyl magnesium chloride solution in diethyl ether (9.7ml, 19.4mmol) was added dropwise at -40°C and the mixture stirred at -40°C for 15 minutes, then cooled to -78°C. Trimethyl borate (2.02g, 2.23ml, 19.4mmol) was added dropwise at -78°C and the reaction was stirred and allowed to warm to room temperature over 2 hours. 2M sodium hydroxide solution (50ml) was

added and the mixture stirred for 15 minutes. The organic layer was re-extracted with 2M sodium hydroxide solution (20ml) and the combined aqueous layers acidified with glacial acetic acid and extracted with diethyl ether (x2). The combined organic phases were washed with water, dried (MgSO_4) and evaporated. The residue was triturated with

5 isohexane, filtered and dried *in vacuo* to give the title compound (2.13g).

^1H NMR (CDCl_3) δ : 5.45(2H, s), 5.71(2H, s), 7.36-7.45(5H, m), 8.09(1H, d), 8.20(1H, d).

[5-Bromo-2-(methyloxy)-3-pyridinyl]boronic acid

10 The title compound was prepared in a similar manner to {5-chloro-2-[(phenylmethyl)oxy]-3-pyridinyl}boronic acid using 3,5-dibromo-2-(methyloxy)pyridine.

^1H NMR (DMSO_d_6) δ : 3.85(3H, s), 7.92(1H, d), 8.11(2H, s), 8.29(1H, d).

[2-[(Phenylmethyl)oxy]-5-(trifluoromethyl)-3-pyridinyl]boronic acid

15 3-Iodo-2-(phenylmethoxy)-5-(trifluoromethyl)pyridine (15.0g, 39.5mmol) was dissolved in tetrahydrofuran (90mL) under nitrogen and cooled to -40°C. Isopropyl magnesium chloride solution in diethyl ether (2.0M, 39.5mL, 79mmol) was added dropwise at -40°C and the mixture stirred at -40°C for 15 minutes, then cooled to -78°C. Trimethyl borate (8.9mL,

20 8.25g, 79.4mmol) was added dropwise at -78°C and the reaction was stirred and allowed to warm to room temperature over 18 hours. 2M aqueous sodium hydroxide solution was added and the layers were separated. The organic phase was dried (MgSO_4) and concentrated *in vacuo*. The residue was triturated with dichloromethane, and the solid material was collected by filtration and dried *in vacuo* to give the title compound (10.53g).

25 LC/MS Rt=3.45min [MH⁺] 298.

2-(2-Bromo-1-cyclopenten-1-yl)-4-chloro-1-(methyloxy)benzene

30 4-Chloro-2-iodoanisole (16.8g, 0.062mol), (2-bromo-1-cyclopenten-1-yl)boronic acid (12g, 0.062 mol), potassium carbonate (35 g, 0.25 mol) and tetrakis(triphenylphosphine)palladium(0) (3.6g, 0.003 mol) were dissolved in toluene-ethanol (1:1 300 mL) and stirred at 90°C, under nitrogen, for 2hrs. Upon cooling, the reaction mixture was poured into water and extracted with ethyl acetate (150mL x 3). The organic layers were dried (MgSO_4), filtered and concentrated. The residue was purified by flash chromatography using 2% ethyl acetate/iso-hexane to give a clear oil that was recrystallized from iso-hexane at 0-4°C to give the required product as a white solid (7.55g).

35 ^1H NMR (CDCl_3) δ : 12.01-2.09(2H, m), 2.65-2.69(2H, m), 2.77-2.81(2H, m), 3.79 (3H, s), 6.79-6.82(1H, m), 7.2-7.25 (2H, m).

40 The following intermediates were prepared by a similar route to 2-(2-bromo-1-cyclopenten-1-yl)-4-chloro-1-(methyloxy)benzene from the appropriate intermediates.

Name	Data
1-(2-Bromo-1-cyclopenten-1-yl)-5-chloro-4-methyl-2-(methyloxy)benzene	¹ H NMR: CDCl ₃ 2.00-2.08(2H, m), 2.34(3H, s), 2.65(2H, t), 2.78(2H, t), 3.78(3H, s), 6.74(1H, s), 7.21(1H, s).
3-(2-Bromo-1-cyclopenten-1-yl)-2-(methyloxy)pyridine	¹ H NMR: (CDCl ₃) δ: 2.03-2.11(2H, m), 2.69-2.74(2H, m), 2.78-2.83(2H, m), 3.95(3H, s), 6.90(1H, dd), 7.58(1H, dd), 8.12(1H, dd).
2-(2-Bromo-1-cyclopenten-1-yl)-1-[(phenylmethyl)oxy]-4-(trifluoromethyl)benzene	¹ H NMR: CDCl ₃ 2.02-2.09(2H, m), 2.70-2.75(2H, t), 2.78-2.82(2H, t), 5.14(2H, s), 6.98(1H, d), 7.33-7.40(5H, m), 7.48(1H, dd), 7.54(1H, d).
2-(2-Bromo-1-cyclopenten-1-yl)-4-chloro-1-[(phenylmethyl)oxy]benzene	¹ H NMR: CDCl ₃ 1.99-2.07(2H, m), 2.67-2.72(2H, t), 2.76-2.81(2H, t), 5.06(2H, s), 6.84(1H, d), 7.18(1H, dd), 7.24-7.38(6H, m).
2-(2-bromo-1-cyclopenten-1-yl)-4,5-dichlorophenyl methyl ether	¹ H NMR: CDCl ₃ 2.01-2.09(2H, m), 2.63-2.65(2H, m), 2.77-2.80(2H, m), 3.79(3H, s), 6.95(1H, s), 7.31(1H, s).

2-(2-Bromo-1-cyclopenten-1-yl)-1-(methyloxy)-4-(trifluoromethyl)benzene

5 [2-Methoxy-5-(trifluoromethyl)phenyl]boronic acid (20g, 90.9mmol), 1,2-dibromocyclopentene (32.5ml, 0.27mol), potassium carbonate (62.8g, 0.45mol) and tetrakis(triphenylphosphine)palladium(0) were refluxed in 1:1 ethanol/toluene (900ml), in the dark, under a nitrogen atmosphere, for 2 hours. After cooling the reaction was filtered over celite and the solvent removed in vacuo, the residue was taken up in ethyl acetate and washed with water and brine, dried over MgSO₄, filtered and concentrated in vacuo to yield a dark oil. This was purified by column chromatography eluting with isohexane. This yielded the title compound as a yellow oil (26.7g, 61%). LC/MS Rt = 3.88.

10

2-(2-Bromo-1-cyclopenten-1-yl)-4-fluoro-1-(methyloxy)benzene

15 Procedure as for 2-(2-bromo-1-cyclopenten-1-yl)-1-(methyloxy)-4-(trifluoromethyl)benzene starting from [5-fluoro-2-(methyloxy)phenyl]boronic acid. LC/MS Rt = 3.70, [MH]⁺ 270.

{2-[2-(Methyloxy)-5-(trifluoromethyl)phenyl]-1-cyclopenten-1-yl}boronic acid

20 2-(2-Bromo-1-cyclopenten-1-yl)-1-(methyloxy)-4-(trifluoromethyl)benzene (26g, 81.3mmol) was dissolved in dry THF (350ml) and the solution cooled to -70°C. n-butyllithium (1.6M solution in hexanes; 101.6ml, 0.16mol) was added slowly keeping the temperature below -

65°C and the reaction allowed to stir for 45 minutes. Tri-isopropyl borate (37.5ml, 0.16mol) was added slowly keeping the temperature below -60°C and the cooling removed and the reaction stirred under nitrogen at RT for a further 15 hours. 2N HCl (300ml) was added and the reaction stirred at RT for a further 2 hours. The reaction was diluted with ethyl acetate and the organics separated, the aqueous washed with ethyl acetate (x3). The combined organics were then washed with brine, dried over MgSO₄, filtered and concentrated in vacuo to yield a yellow oil. This was purified by column chromatography on a 75L Biotage column eluting in 40% ethyl acetate/isohexane. This yielded the title compound as a white solid. LC/MS Rt = 2.96.

10 The following intermediates were prepared by a similar route to {2-[2-(methyloxy)-5-(trifluoromethyl)phenyl]-1-cyclopenten-1-yl}boronic acid from the appropriate intermediates.

Name	Data
{2-[2-(Methyloxy)phenyl]-1-cyclopenten-1-yl}boronic acid	LC/MS Rt = 3.69 min. [2MH ⁺] 417.2
{2-[5-Fluoro-2-(methyloxy)phenyl]-1-cyclopenten-1-yl}boronic acid	LC/MS Rt = 2.52 min.
{2-[5-Chloro-2-(methyloxy)phenyl]-1-cyclopenten-1-yl}boronic acid	¹ H NMR (CDCl ₃) δ: 1.91-1.98 (2H, m), 2.66-2.73 (4H, m), 3.80 (3H, s), 4.30 (2H, s), 6.85 (1H, s), 7.16 (1H, s), 7.21 (1H, dd).
{2-[2-[(Phenylmethyl)oxy]-5-(trifluoromethyl)phenyl]-1-cyclopenten-1-yl}boronic acid	LC/MS: Rt = 3.44 min, [M+H ₂ O] 380, [2M] 724
{2-[5-Chloro-4-methyl-2-(methyloxy)phenyl]-1-cyclopenten-1-yl}boronic acid	¹ H NMR (CDCl ₃) δ: 1.90-1.97(2H, m), 2.36(3H, s), 2.65-2.71(4H, m), 3.79(3H, s), 4.41(2H, s), 6.78(1H, s), 7.14(1H, s).
(2-[5-Chloro-2-[(phenylmethyl)oxy]phenyl]-1-cyclopenten-1-yl)boronic acid	LC/MS: Rt = 3.39 min, [2MH] 637
{2-[4,5-dichloro-2-(methyloxy)phenyl]-1-cyclopenten-1-yl}boronic acid	LCMS: Rt = 3.13min

15 5-(2-Bromo-1-cyclopenten-1-yl)-N-(1,1-dimethylethyl)-3-pyridazinecarboxamide

(2-Bromo-1-cyclopenten-1-yl)boronic acid (0.6g, 3.2mmol), N-(1,1-dimethylethyl)-5-iodo-3-pyridazinecarboxamide (1.0g, 3.2mmol), tetrakis(triphenylphosphine)palladium(0) (200mg, 0.172mmol) and potassium carbonate (1.1g, 8mmol) in toluene/ethanol (1:1, 10ml) were refluxed overnight under nitrogen in the

dark. The reaction mixture was then filtered through celite, and chromatographed with diethyl ether/iso-hexane gradient giving (0.78g, 71% yield).

LC/MS Rt=3.13min [MH⁺] 326, 327

5 Ethyl 6-(2-bromo-1-cyclopenten-1-yl)-3-chloro-2-pyridinecarboxylate

A mixture of ethyl 3,6-dichloro-2-pyridinecarboxylate (220mg, 1mmol), (2-bromo-1-cyclopenten-1-yl)boronic acid (191mg, 1mmol), potassium carbonate (552mg, 4mmol) and tetrakis(triphenylphosphine)palladium(0) (58mg, 0.05mmol) in 1:1 ethanol/toluene (4ml)

10 was stirred and heated at 90°C under nitrogen for 2 hours. after cooling the mixture was dissolved in diethyl ether/water and the organic phase dried (magnesium sulphate) evaporated and the residue purified by chromatography on silica eluting with ethyl acetate/iso-hexane (1:19) to give 110mg of colourless oil.

LC/MS t=3.81, [MH⁺] 332.3.

15

The following compounds were prepared by a similar route to ethyl 6-(2-bromo-1-cyclopenten-1-yl)-3-chloro-2-pyridinecarboxylate from the appropriate intermediates.

Name	Data
Ethyl 6-(2-bromo-1-cyclopenten-1-yl)-2-pyrazinecarboxylate	LC/MS: Rt = 3.07min. [M+H] = 297, 299.
Ethyl 6-(2-bromo-1-cyclopenten-1-yl)-2-pyridinecarboxylate	LC/MS: Rt = 3.27 min.[M+H] = 296,298.
Ethyl 3-(2-bromo-1-cyclopenten-1-yl)benzoate	Rt = 3.98 min. [MH ⁺] 295, 297.
Ethyl 5-(2-bromo-1-cyclopenten-1-yl)-2-methylbenzoate	¹ H NMR (CDCl ₃) δ: 1.39(3H, t), 2.01-2.08(2H, m), 2.59(3H, s), 2.77(2H,m), 2.85(2H, m), 4.36(2H, q), 7.24(1H, t), 7.65(1H, d), 8.12(1H, s).
Ethyl 5-(2-bromo-1-cyclopenten-1-yl)-2-fluorobenzoate	Rt = 3.82min. [MH ⁺] 313, 315.
Ethyl 3-(2-bromo-1-cyclopenten-1-yl)-5-fluorobenzoate	Rt = 3.91min. [MH ⁺] 313, 315.
Ethyl 3-amino-5-(2-bromocyclopent-1-enyl)benzoate	LC/MS Rt=3.51min [MH ⁺] 310,312.

Ethyl 2-amino-5-(2-bromo-1-cyclopenten-1-yl)benzoate	¹ H NMR (CDCl ₃) δ: 1.39 (3H, t, J=7Hz), 1.98-2.06 (2H, m), 2.71-2.76 (2H, m), 2.81-2.86 (2H, m) 4.33 (2H, q, J=7Hz), 5.80 (2H, br s), 6.65 (1H, d, J=9Hz), 7.65 (1H, dd, J=9Hz, 2Hz), 8.14 (1H, d, J=2Hz).
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Ethyl 5-(2-bromocyclopent-1-enyl)-2-fluorobenzoate

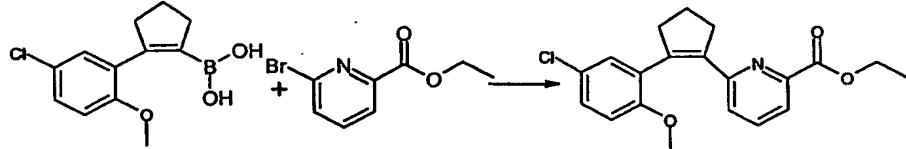
Ethyl 2-fluoro-5-iodobenzoate (4.7g, 16.0mmol), 2-bromo-cyclopent-1-enylboronic acid (3.06g, 16.0mmol), potassium carbonate (15.5g, 112mmol) and Pd(PPh₃)₄ (0.925g, 0.8mmol) were dissolved in toluene-ethanol (1:1, 110mL) and stirred at 100°C under nitrogen for 1.5 hours. Upon cooling, the reaction mixture was diluted with diethyl ether, and washed with water. The aqueous layer was extracted with further diethyl ether, and the combined organic extracts were dried (MgSO₄), and concentrated *in vacuo*. The residue was purified by flash chromatography on silica (gradient elution, 1-5% ethyl acetate/cyclohexane) to give the required product as a yellow oil (3.84g). LC/MS Rt=3.80min [MH⁺] 313, 315.

Ethyl 3-(2-bromocyclopent-1-enyl)-5-fluorobenzoate

Ethyl 3-bromo-5-fluorobenzoate (5.17g, 20.9mmol), 2-bromo-cyclopent-1-enylboronic acid (3.99g, 20.9mmol), potassium carbonate (23g, 167mmol) and Pd(PPh₃)₄ (1.1g, 1.0mmol) were dissolved in toluene-ethanol (1:1, 150mL) and heated to reflux for 1.5 hours under a nitrogen atmosphere. Upon cooling, the reaction mixture was diluted with diethyl ether, and washed with water. The aqueous layer was extracted with further diethyl ether, and the combined organic extracts were dried (Na₂SO₄), and concentrated *in vacuo*. The residue was purified by flash chromatography on silica (gradient elution, 0-5% ethyl acetate/cyclohexane) to give the required product as a yellow oil (5.93g). LC/MS Rt=3.93min [MH⁺] 313, 315.

Ethyl 3-amino-5-(2-bromocyclopent-1-enyl)benzoate

Ethyl 3-amino-5-iodobenzoate (3.66g, 12.6mmol), 2-bromo-cyclopent-1-enylboronic acid (2.41g, 12.6mmol), potassium carbonate (12.2g, 88.2mmol) and Pd(PPh₃)₄ (0.73g, 0.63mmol) were dissolved in toluene-ethanol (1:1, 50mL) and heated to reflux for 1.75 hours under a nitrogen atmosphere. After cooling, the reaction mixture was diluted with diethyl ether, and washed with water. The aqueous layer was extracted with further diethyl ether, and the combined organic extracts were dried (Na₂SO₄), and concentrated *in vacuo*. The residue was purified by flash chromatography on silica (gradient elution, 0-5% ethyl acetate/cyclohexane) to give the required product (4.21g). LC/MS Rt=3.51min [MH⁺] 310,312.

Ethyl 6-[2-[5-chloro-2-(methyloxy)phenyl]-1-cyclopenten-1-yl]-2-pyridinecarboxylate

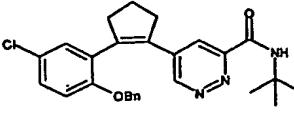
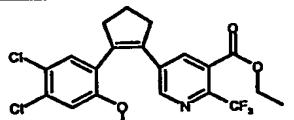
5 A mixture of ethyl 6-bromo-2-pyridinecarboxylate (4.1g, 17.8 mmol), {2-[5-chloro-2-(methyloxy)phenyl]-1-cyclopenten-1-yl}boronic acid (4.1g, 16 mmol), potassium carbonate (11.2g, 81 mmol) and tetrakis(triphenylphosphine)palladium(0) (1.88g, 1.6mmol) was stirred and heated in 1:1 toluene/ethanol (50 ml) at 90°C under nitrogen for 2 hours. After cooling the mixture was diluted with ethyl acetate/water and the organic phase dried (magnesium sulphate), evaporated to dryness and the residue purified by chromatography (12% ethyl acetate in iso-hexane) to yield the title compound as a clear oil (4g).

10 LC/MS: Rt 3.8 [MH⁺] 358,361

15 The following compounds were prepared by a similar route to ethyl 6-[2-[5-chloro-2-(methyloxy)phenyl]-1-cyclopenten-1-yl]-2-pyridinecarboxylate from the appropriate intermediates.

	Name	Data
	Ethyl 6-[2-[2-(methyloxy)phenyl]-1-cyclopenten-1-yl]-2-pyridinecarboxylate	LC/MS: Rt = 3.53 min, [M+H] 324.
	Ethyl 6-[2-[2-(methyloxy)phenyl]-1-cyclopenten-1-yl]-2-pyrazinecarboxylate	LC/MS: Rt = 3.47 min, [M+H] 325.
	Ethyl 6-[2-[5-chloro-2-(methyloxy)phenyl]-1-cyclopenten-1-yl]-3-methyl-2-pyridinecarboxylate	LC/MS Rt=3.98, [MH ⁺] 372.4, 374.5
	Ethyl 3-methyl-6-[2-[2-[(phenylmethyl)oxy]-5-(trifluoromethyl)phenyl]-1-cyclopenten-1-yl]-2-pyridinecarboxylate	LC/MS: Rt = 4.39 min, [M+H] 482.

	Ethyl 3-chloro-6-{2-[5-chloro-2-(methyoxy)phenyl]-1-cyclopenten-1-yl}-2-pyridinecarboxylate	LC/MS Rt=3.95, [MH+] 392.4
	Methyl 5-(2-[5-chloro-2-[(phenylmethyl)oxy]phenyl]-1-cyclopenten-1-yl)-2-(trifluoromethyl)-3-pyridinecarboxylate	LC/MS Rt=4.20, [MH+] 488.4
	Ethyl 3-chloro-6-{2-[2-[(phenylmethyl)oxy]-5-(trifluoromethyl)phenyl]-1-cyclopenten-1-yl}-2-pyridinecarboxylate	LC/MS Rt=4.15, [MH+] 502.4, 504.4
	Ethyl 6-{2-[5-chloro-2-(methyoxy)phenyl]-1-cyclopenten-1-yl}-3-pyridinecarboxylate	LC/MS Rt=3.84, [MH+] 358.3
	Ethyl 6-{2-[5-chloro-4-methyl-2-(methyoxy)phenyl]-1-cyclopenten-1-yl}-2-pyridinecarboxylate	LC/MS: Rt = 3.77 min. [M+H] = 372.
	Ethyl 5-{2-[2-[(phenylmethyl)oxy]-5-(trifluoromethyl)phenyl]-1-cyclopenten-1-yl}-2-(trifluoromethyl)-3-pyridinecarboxylate	LC/MS: Rt = 3.91 min. [M+H] = 536
	Ethyl 2-(2-[5-chloro-2-[(phenylmethyl)oxy]phenyl]-1-cyclopenten-1-yl)-3-pyridinecarboxylate	LC/MS: Rt = 3.89 min. [M+H] = 434, 436
	Ethyl 6-(2-[5-chloro-2-[(phenylmethyl)oxy]phenyl]-1-cyclopenten-1-yl)-4-(trifluoromethyl)-2-pyridinecarboxylate	LC/MS: [M+H] 502.4, 504.4, Rt=4.58min
	Methyl 6-(2-[5-chloro-2-[(phenylmethyl)oxy]phenyl]-1-cyclopenten-1-yl)-4-pyrimidinecarboxylate	LC/MS: Rt = 3.74min [M+H] 421, 423

	5-(2-{5-Chloro-2-[(phenylmethyl)oxy]phenyl}-1-cyclopenten-1-yl)-N-(1,1-dimethylethyl)-3-pyridazinecarboxamide	LC/MS: Rt = 3.98min [M+H] 462, 464
	<u>Ethyl 5-{2-[4,5-dichloro-2-(methyoxy)phenyl]-1-cyclopenten-1-yl}-2-(trifluoromethyl)-3-pyridinecarboxylate</u>	LC/MS: Rt = 3.68min [M+H] 392

Methyl 5-{2-[5-chloro-2-(methyoxy)phenyl]-1-cyclopenten-1-yl}-2-ethyl-3-pyridinecarboxylate

5

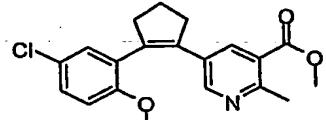
A mixture of {2-[5-chloro-2-(methyoxy)phenyl]-1-cyclopenten-1-yl}boronic acid (2.53 g, 10 mmol), methyl 5-chloro-2-ethyl-3-pyridinecarboxylate (1.995 g, 10 mmol), palladium acetate (22 mg, 0.0909 mmol), potassium fluoride on alumina (40%) (4.35 g, 30 mmol) and (di-tert-butylphosphino)biphenyl (60 mg, 0.20 mmol) in anhydrous tetrahydrofuran (25 ml) was heated at 50°C under an atmosphere of nitrogen for 3 hours. The reaction mixture was cooled to room temperature and diluted with diethyl ether and water. The ether layer was separated, dried over magnesium sulphate and evaporated to dryness. The residue was purified using flash chromatography eluting with ethyl acetate/ iso-hexane (15%) to give the title compound as a yellow oil. 1.93 g, 52%.

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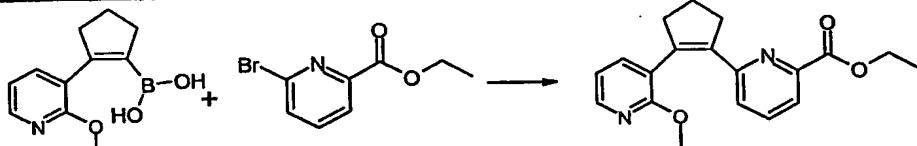
¹H NMR (CDCl₃) δ: 1.24 (3H, t), 2.06-2.14 (2H, m), 2.81-2.56 (2H, m), 2.91-2.95 (2H, m), 3.08 (2H, q), 3.63 (3H, s), 3.85 (3H, s), 6.79 (1H, d), 7.00 (1H, d), 7.18 (1H, dd,), 7.91 (1H, d), 8.34 (1H, d). LC/MS: Rt = 3.83 min, [M+H] 372.

10

The following intermediates were prepared by a similar route to methyl 5-{2-[5-chloro-2-(methyoxy)phenyl]-1-cyclopenten-1-yl}-2-ethyl-3-pyridinecarboxylate from the appropriate intermediates.

	Name	Data
	Methyl 5-{2-[5-chloro-2-(methyoxy)phenyl]-1-cyclopenten-1-yl}-2-methyl-3-pyridinecarboxylate	LC/MS Rt=3.64, [MH+] 358.4, 360.4

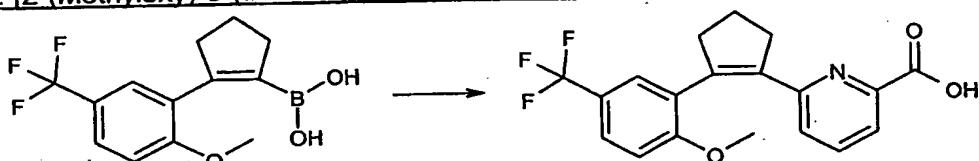
	Methyl 5-(2-{5-chloro-2-[(phenylmethyl)oxy]phenyl}-1-cyclopenten-1-yl)-2-methyl-3-pyridinecarboxylate	LC/MS Rt=4.06, [MH+] 334.4, 436.4
	Methyl 2-methyl-5-{2-[2-((phenylmethyl)oxy)-5-(trifluoromethyl)phenyl]-1-cyclopenten-1-yl}-3-pyridinecarboxylate	LC/MS Rt=4.04, [MH+] 468.4
	Methyl 2-ethyl-5-{2-[2-((phenylmethyl)oxy)-5-(trifluoromethyl)phenyl]-1-cyclopenten-1-yl}-3-pyridinecarboxylate	LC/MS Rt=4.17, [MH+] 482.5

Ethyl 6-{2-[2-(methyloxy)-3-pyridinyl]-1-cyclopenten-1-yl}-2-pyridinecarboxylate

5 {2-[2-(Methyloxy)-3-pyridinyl]-1-cyclopenten-1-yl}boronic acid (219mg, 1mmol) and ethyl 6-bromo-2-pyridinecarboxylate (230mg, 1mmol) were dissolved in toluene/ethanol (1:1, 10ml) under nitrogen and tetrakis(triphenylphosphine)palladium(0) (58mg, 0.05mmol) and potassium carbonate (1.104g, 8mmol) added. The mixture was heated at 80°C in a Smithcreator® microwave for 20 minutes. Diethyl ether and water were added and the organic layer washed with water, dried (MgSO_4) and evaporated. The brown oil was purified by flash chromatography, eluting with 5-20% ethyl acetate/isohexane to give the title compound (120mg).

10 ^1H NMR (CDCl_3) δ : 1.38(3H, t), 2.07-2.15(2H, m), 2.87-2.92(2H, m), 3.09-3.14(2H, m), 3.78(3H, s), 4.38(2H, q), 6.78(1H, dd), 7.08(1H, d), 7.33(1H, dd), 7.54(1H, t), 7.84(1H, d), 8.07(1H, dd).

15 6-{2-[2-(Methyloxy)-5-(trifluoromethyl)phenyl]-1-cyclopenten-1-yl}-2-pyridinecarboxylic acid



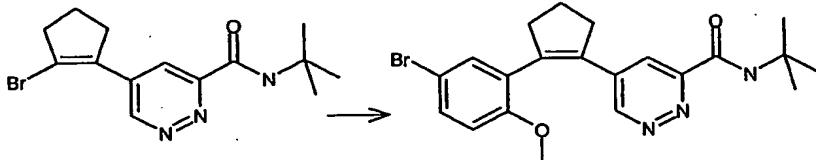
20 {2-[2-(Methyloxy)-5-(trifluoromethyl)phenyl]-1-cyclopenten-1-yl}boronic acid (5.5g, 19.2mmol), ethyl 6-bromopyridine-2-carboxylate (4.42g, 19.2mmol), potassium carbonate (13.29g, 96.2mmol) and tetrakis(triphenylphosphine)palladium(0) were refluxed in 1:1

ethanol/toluene (200ml) under nitrogen in the dark for 16 hours. After cooling the reaction was filtered over celite and the solvent removed in vacuo, the residue was taken up in ethyl acetate and washed with water and brine, dried over MgSO₄, filtered and concentrated in vacuo to yield a yellow solid. This was purified by column chromatography eluting in 50% ethyl acetate/isohexane. This yielded the title compound as a yellow solid (5.51g, 79%). LC/MS Rt = 3.22, [MH⁺] 364.

The following compounds were prepared by a similar route to 6-{2-[2-(methyloxy)-5-(trifluoromethyl)phenyl]-1-cyclopenten-1-yl}-2-pyridinecarboxylic acid from the appropriate intermediates.

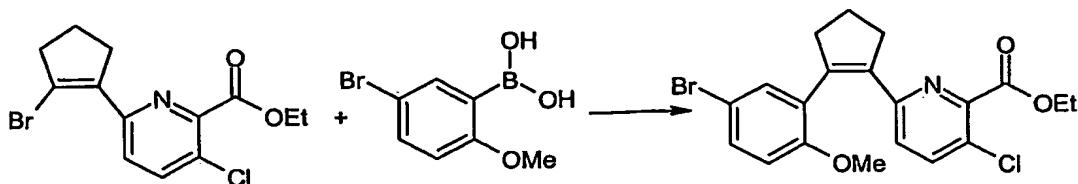
	Name	LC/MS
	6-{2-[2-(Methyloxy)-5-(trifluoromethyl)phenyl]-1-cyclopenten-1-yl}-2-pyridinecarboxylic acid	t = 3.66, [MH ⁺] 365
	6-{2-[5-Fluoro-2-(methyloxy)phenyl]-1-cyclopenten-1-yl}-2-pyridinecarboxylic acid	t = 2.70min, [MH ⁺] 314
	6-{2-[5-Fluoro-2-(methyloxy)phenyl]-1-cyclopenten-1-yl}-2-pyridinecarboxylic acid	t = 3.59min, [MH ⁺] 315

5-{2-[5-Bromo-2-(methyloxy)phenyl]-1-cyclopenten-1-yl}-N-(1,1-dimethylethyl)-3-pyridazinecarboxamide



5-(2-Bromo-1-cyclopenten-1-yl)-N-(1,1-dimethylethyl)-3-pyridazinecarboxamide (8.3g, 25.5mmol), 5-bromo-2-(methyloxy)phenylboronic acid (6.9g, 30mmol), tetrakis(triphenylphosphine)palladium(0) (1.51g, 1.3mmol) and potassium carbonate(8.0g, 57.97mmol) in dimethoxyethane (60ml) were refluxed overnight under nitrogen, in the dark. The reaction mixture was then filtered through celite and chromatographed giving the title compound (7.0g, 65% yield). LC/MS Rt=3.71mins [MH⁺] 432, 433.

Ethyl 6-{2-[5-bromo-2-(methyloxy)phenyl]-1-cyclopenten-1-yl}-3-chloro-2-pyridinecarboxylate



A mixture of ethyl 6-(2-bromo-1-cyclopenten-1-yl)-3-chloro-2-pyridinecarboxylate (110mg, 0.33mmol), 5-bromo-2-(methyoxy)phenylboronic acid (77mg, 0.33mmol), potassium carbonate (276mg, 2mmol) and tetrakis(triphenylphosphine)palladium(0) (38mg, 0.033mmol) in 1,2-dimethoxyethane (4ml) was stirred and heated at 70°C under nitrogen for 2 hours when a further portion of 5-bromo-2-methoxyphenylboronic acid (77mg, 0.33mmol) was added. After heating for a further 2 hours the mixture was cooled, dissolved in diethyl ether/water and the organic phase dried (magnesium sulphate) evaporated and the residue purified by chromatography on silica eluting with ethyl acetate/iso-hexane (7:93) to give 110mg of colourless oil.

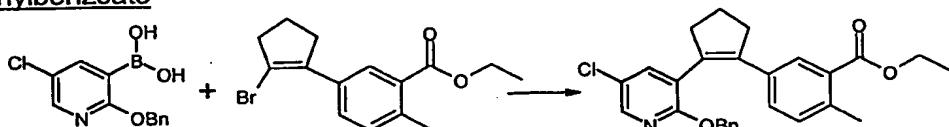
LC/MS Rt=4.14, [MH⁺] 438.3.

The following compounds were prepared by a similar route to ethyl 6-{2-[5-bromo-2-(methyoxy)phenyl]-1-cyclopenten-1-yl}-3-chloro-2-pyridinecarboxylate from the appropriate intermediates.

	Name	Data
	Ethyl 6-{2-[5-bromo-2-(methyoxy)phenyl]-1-cyclopenten-1-yl}-2-pyridinecarboxylate	LC/MS: Rt = 3.80 min. [M+H] = 402, 404.
	Ethyl 6-{2-[5-bromo-2-(methyoxy)phenyl]-1-cyclopenten-1-yl}-2-pyrazinecarboxylate	LC/MS: Rt = 3.66min. [M+H] = 403, 405.

Ethyl 5-(2-{5-chloro-2-[(phenylmethyl)oxy]-3-pyridinyl}-1-cyclopenten-1-yl)-2-methylbenzoate

20 {5-Chloro-2-[(phenylmethyl)oxy]-3-pyridinyl}boronic acid (247mg, 0.938mmol) and ethyl 5-(2-bromo-1-cyclopenten-1-yl)-2-methylbenzoate (290mg, 0.938mmol) were dissolved in toluene/ethanol (1:1, 4ml) under nitrogen and tetrakis(triphenylphosphine)palladium(0) (54mg, 0.047mmol) and potassium carbonate (1.04g, 7.5mmol) added. The mixture was heated at 80°C in a Smithcreator® microwave for 10 minutes. Diethyl ether and water were added and the organic layer washed with water, dried ($MgSO_4$) and evaporated. The

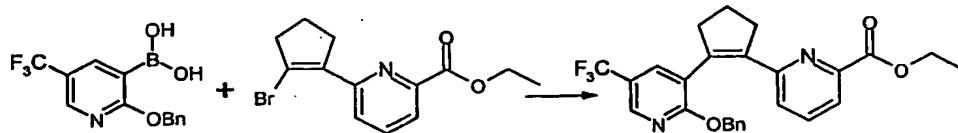


brown oil was purified by flash chromatography, eluting with 3% ethyl acetate/isohexane to give the title compound (262mg). LC/MS Rt=4.47min [MH⁺] 448, 450.

5 The following compounds were prepared by a similar route to ethyl 5-(2-{5-chloro-2-[(phenylmethyl)oxy]-3-pyridinyl}-1-cyclopenten-1-yl)-2-methylbenzoate from the appropriate intermediates.

	COMPOUND NAME	¹ H NMR/LCMS
	Ethyl 5-(2-{5-chloro-2-[(phenylmethyl)oxy]-3-pyridinyl}-1-cyclopenten-1-yl)-2-fluorobenzoate	(CDCl ₃) δ: 1.33(3H, t), 2.05-2.08(2H, m), 2.82-2.91(4H, m), 4.31(2H, q), 5.27(2H, s), 6.84(1H, dd), 7.11(1H, m), 7.22-7.29(6H, m), 7.66(1H, dd), 8.00(1H, d)
	Ethyl 5-(2-{5-chloro-2-[(phenylmethyl)oxy]-3-pyridinyl}-1-cyclopenten-1-yl)-3-fluorobenzoate	(CDCl ₃) δ: 1.32(3H, t), 2.04-2.11(2H, m), 2.83-2.92(4H, m), 4.29(2H, q), 5.26(2H, s), 6.89(1H, dd), 7.21-7.56(8H, m), 8.01(1H, d)
	Ethyl 2-fluoro-5-{2-[2-(methyoxy)-3-pyridinyl]-1-cyclopenten-1-yl}benzoate	(CDCl ₃) δ: 1.34(3H, t), 2.05-2.12(2H, m), 2.83-2.87(2H, m), 2.89-2.94(2H, m), 3.85(3H, s), 4.32(2H, q), 6.77(1H, dd), 6.88(1H, dd), 7.15(1H, td), 7.24(1H, dd), 7.69(1H, dd), 8.07(1H, dd).
	Ethyl 2-fluoro-5-{2-[2-[(phenylmethyl)oxy]-5-(trifluoromethyl)-3-pyridinyl]-1-cyclopenten-1-yl}benzoate	Rt = 4.42min. [MH ⁺] 486
	Ethyl 5-{2-[5-bromo-2-(methyoxy)-3-pyridinyl]-1-cyclopenten-1-yl}-2-fluorobenzoate	Rt = 4.10min. [MH ⁺] 420, 422.

10 Ethyl 6-{2-[2-[(phenylmethyl)oxy]-5-(trifluoromethyl)-3-pyridinyl]-1-cyclopenten-1-yl}-2-pyridinecarboxylate

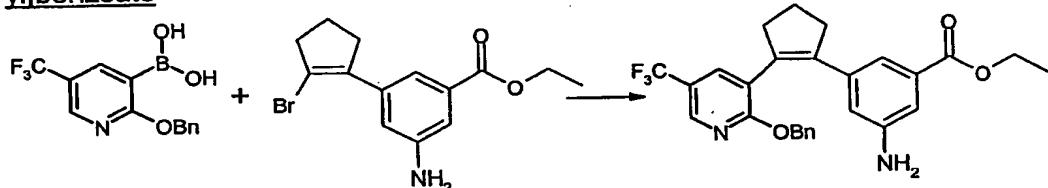


[2-[(Phenylmethyl)oxy]-5-(trifluoromethyl)-3-pyridinyl]boronic acid (3.71g, 12.5mmol) and 6-(2-bromocyclopent-1-enyl)-pyridine-2-carboxylic acid ethyl ester (1.85g, 6.25mmol) were dissolved in dioxane (75mL) under nitrogen together with

5 tris(dibenzylideneacetone)dipalladium(0) (86mg, 0.094mmol), tri(*t*-butyl)phosphonium tetrafluoroborate (82mg, 0.28mmol) and potassium fluoride (1.19g, 20.5mmol). The mixture was heated at 100°C for 3 hours. After cooling, the dioxane was removed *in vacuo* and the residue was partitioned between diethyl ether and water. The aqueous was extracted with further ether, dried (Na_2SO_4) and concentrated *in vacuo*. The resulting brown oil was purified by flash chromatography on silica (gradient elution, 0-3% ethyl acetate/cyclohexane) to give the title compound (871mg).

10 LC/MS Rt=4.09min [MH^+] 469.

Ethyl 3-amino-5-{2-[2-(phenylmethoxy)-5-(trifluoromethyl)pyridin-3-yl]cyclopent-1-en-1-yl}benzoate

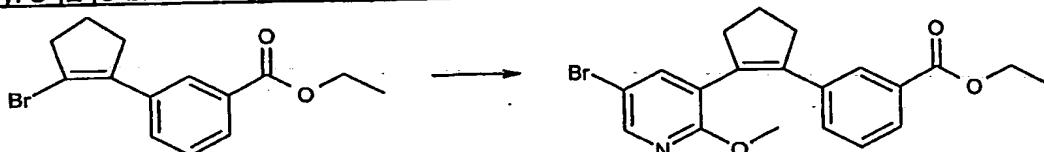


15 2-(Phenylmethoxy)-5-(trifluoromethyl)pyridine-3-boronic acid (6.0g, 20.2mmol) and ethyl 3-amino-5-(2-bromocyclopent-1-enyl)benzoate (3.16g, 10.1mmol) were dissolved in dimethoxyethane (50mL) under nitrogen, and tetrakis(triphenylphosphine)palladium(0)

20 (0.58g, 0.5mmol) and 2N aqueous sodium carbonate solution (10ml) were added. The mixture was heated at 80°C for 18 hours. After cooling, the solvents were removed *in vacuo*, and the residue was partitioned between diethyl ether and water. The aqueous was extracted with further ether (x2), and the combined organic layers were dried (Na_2SO_4) and concentrated *in vacuo*. The resulting dark brown oil was purified using an acidic solid phase cartridge (Isolute® Flash SCX-2, 50g), loading the crude material as a methanol solution and eluting with 10% aqueous ammonia in methanol. Concentration of the relevant fractions *in vacuo* gave the title compound (4.01g).

25 LC/MS Rt=4.01min [MH^+] 483.

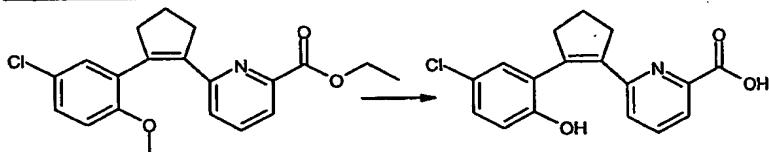
30 Ethyl 3-{2-[5-bromo-2-(methyloxy)-3-pyridinyl]-1-cyclopenten-1-yl}benzoate



Ethyl 3-(2-bromo-1-cyclopenten-1-yl)benzoate (0.5g, 1.7mmol), [5-bromo-2-(methyloxy)-3-pyridinyl]boronic acid (0.45g, 1.7mmol), potassium carbonate (1.2g, 8.5mmol) and 1,2-dimethoxyethane (10ml) were combined and degassed for 15 minutes.

5 tetrakis(triphenylphosphine)palladium(0) (0.2g, 0.17mmol) was added and the reaction stirred under a nitrogen atmosphere in the dark at 80°C for 3 hours. A further equivalent of [5-bromo-2-(methyloxy)-3-pyridinyl]boronic acid (0.45g, 1.7mmol) was added and the reaction continued under the above conditions for a further 14 hours. A further equivalent of [5-bromo-2-(methyloxy)-3-pyridinyl]boronic acid (0.45g, 1.7mmol) and a further equivalent of tetrakis(triphenylphosphine)palladium(0) (0.2g, 0.17mmol) was added and 10 the reaction continued under the above conditions for a further 24 hours. The reaction was then filtered through celite and the solvent removed *in vacuo*. The residue was purified by column chromatography eluting with 10% diethyl ether/iso hexane. This yielded the title compound as a clear oil (0.201g, 30%). LC/MS Rt = 4.30 [MH⁺] 402/404.

15 6-[2-(5-Chloro-2-hydroxyphenyl)-1-cyclopenten-1-yl]-2-pyridinecarboxylic acid



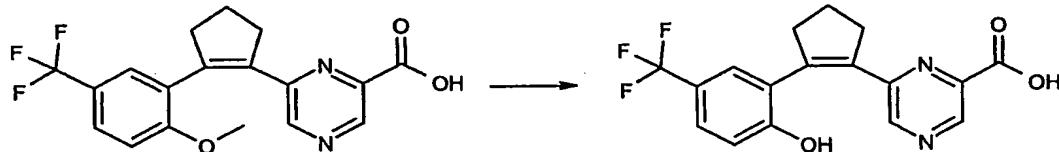
20 Ethyl 6-{2-[5-chloro-2-(methyloxy)phenyl]-1-cyclopenten-1-yl}-2-pyridinecarboxylate (3.9g, 0.011mol) and sodium methanethiolate (4g, 0.055 mol) in dry DMF (40 ml) were heated at 100°C under nitrogen for 5h. After cooling the mixture was poured into water and washed with diethyl ether. The aqueous phase was then acidified with acetic acid and extracted with ethyl acetate (50ml x 3). The combined organic layers were dried (magnesium sulphate) and evaporated. The residue was redissolved in toluene and evaporated again to give a yellow solid that was triturated with diethyl ether to give the title compound as a yellow oil (2.6g, 76%). LC/MS: Rt 2.85 [MH⁺] 316,318.

25 The following intermediates were prepared by a similar route to 6-[2-(5-chloro-2-hydroxyphenyl)-1-cyclopenten-1-yl]-2-pyridinecarboxylic acid from the appropriate intermediates.

Structure	Name	Data
	6-[2-(2-Hydroxyphenyl)-1-cyclopenten-1-yl]-2-pyridinecarboxylic acid	LC/MS: Rt = 2.20 min, [M+H] 282.
	5-[2-(5-Chloro-2-hydroxyphenyl)-1-cyclopenten-1-yl]-2-ethyl-3-pyridinecarboxylic acid	LC/MS: Rt=2.99 min, [M+H] 344.

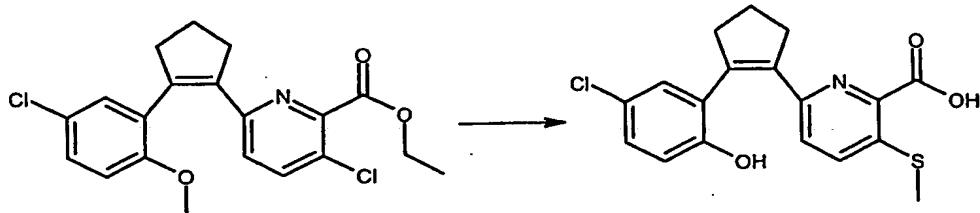
	5-[2-(5-Chloro-2-hydroxyphenyl)-1-cyclopenten-1-yl]-2-methyl-3-pyridinecarboxylic acid	LC/MS Rt=2.80 min, [MH ⁺] 330.4, 332.4
	6-[2-(5-Chloro-2-hydroxyphenyl)-1-cyclopenten-1-yl]-3-pyridinecarboxylic acid	LC/MS Rt=3.70 min, [MH ⁺] 316.3, 318.4
	6-[2-(5-Bromo-2-hydroxyphenyl)-1-cyclopenten-1-yl]-2-pyrazinecarboxylic acid	LC/MS: Rt=4.37 min. [M+H] = 361, 363.
	6-[2-(5-Chloro-2-hydroxy-4-methylphenyl)-1-cyclopenten-1-yl]-2-pyridinecarboxylic acid	LC/MS: Rt=3.02 min. [M+H] = 330
	5-[2-(4,5-dichloro-2-hydroxyphenyl)-1-cyclopenten-1-yl]-2-(trifluoromethyl)-3-pyridinecarboxylic acid	LC/MS: Rt=3.17 min. [M+H] = 418

6-[2-(2-Hydroxy-5-(trifluoromethyl)phenyl)-1-cyclopenten-1-yl]-2-pyrazinecarboxylic acid



5 6-[2-(2-Hydroxy-5-(trifluoromethyl)phenyl)-1-cyclopenten-1-yl]-2-pyrazinecarboxylic acid (1.92g, 5.27mmol), sodium methanethiolate (1.87g, 26.4mmol) and DMF (40ml) were heated to 75°C for 4.5 hours. After cooling the reaction was diluted with ethyl acetate washed with water and brine. The organic layer was dried over MgSO₄, filtered and concentrated in vacuo to yield a yellow solid (1.66g). LC/MS Rt = 3.57, [MH⁺] 351.

10 6-[2-(5-Chloro-2-hydroxyphenyl)-1-cyclopenten-1-yl]-3-(methylthio)-2-pyridinecarboxylic acid



A mixture of ethyl 3-chloro-6-{2-[5-chloro-2-(methyloxy)phenyl]-1-cyclopenten-1-yl}-2-pyridinecarboxylate (960mg, 2.49mmol) and sodium methanethiolate (857mg, 12.25mmol) in dimethylformamide (10ml) was stirred and heated at 100°C under nitrogen for 4 hours.

5 After cooling the mixture was diluted with diethyl ether/water and the aqueous separated, acidified with acetic acid and extracted with ether which was washed three times with water then dried (magnesium sulphate) evaporated and triturated with ether to give an orange solid (695mg). LC/MS Rt=3.46, [MH⁺] 362.4, 364.4.

6-[2-Hydroxy-5-(trifluoromethyl)phenyl]cyclopent-1-en-1-yl}pyridine-2-carboxylic acid

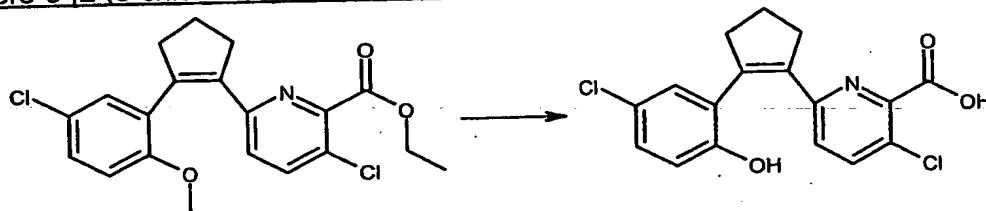


10 6-[2-Methoxy-5-(trifluoromethyl)phenyl]cyclopent-1-en-1-yl}pyridine-2-carboxylic acid (2g, 5.5mmol) was dissolved in anhydrous dichloromethane (80ml) and cooled to -70°C. Boron tribromide (5ml, 55mmol) was added slowly and the reaction allowed to warm to -3°C and stirred under nitrogen for 19 hours. The reaction was quenched with ice and then 15 water and stirred vigorously for 30 minutes. The aqueous layer was washed with dichloromethane (x2), the combined organic layers were washed with brine, dried over MgSO₄, filtered and concentrated in vacuo to yield the title compound as a dark solid (2.13g). LC/MS Rt = 3.07min, [MH⁺] 350.

20 The following intermediates were prepared by a similar route to 6-[2-hydroxy-5-(trifluoromethyl)phenyl]cyclopent-1-en-1-yl}pyridine-2-carboxylic acid from the appropriate intermediates.

	Name	LC/MS
	6-[2-(5-Fluoro-2-hydroxyphenyl)-1-cyclopenten-1-yl]2-pyridinecarboxylic acid	Rt = 2.50min [MH ⁺] 300.
	6-[2-(5-Fluoro-2-hydroxyphenyl)-1-cyclopenten-1-yl]2-pyrazinecarboxylic acid	Rt = 3.53min [MH ⁺] 301.

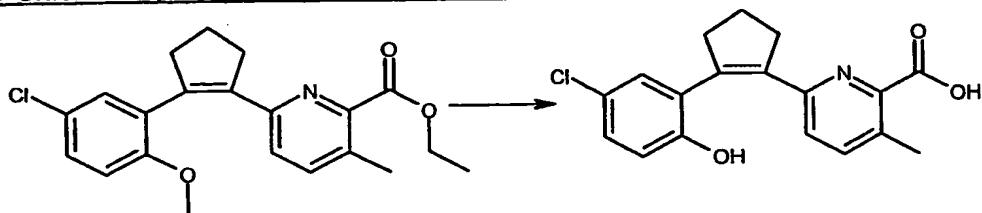
25 3-Chloro-6-[2-(5-chloro-2-hydroxyphenyl)-1-cyclopenten-1-yl]-2-pyridinecarboxylic acid



A solution of ethyl 3-chloro-6-[2-[5-chloro-2-(methyloxy)phenyl]-1-cyclopenten-1-yl]-2-pyridinecarboxylate (2.35g, 6mmol) in dichloromethane (15ml) was cooled to -50°C and 1M boron tribromide in dichloromethane (20ml) was added.

5 The mixture was allowed to warm to room temperature and after 3 hours was poured onto ice and basified with 2M sodium hydroxide solution then acidified with acetic acid. The organic layer was separated, dried (magnesium sulphate), toluene (30ml) added and evaporated to give a yellow gum (2.16g). LC/MS t=4.09, [MH⁺] 350.4

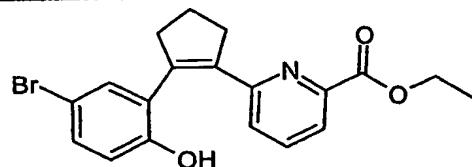
6-[2-(5-Chloro-2-hydroxyphenyl)-1-cyclopenten-1-yl]-3-methyl-2-pyridinecarboxylic acid



10

Procedure as for 3-chloro-6-[2-(5-chloro-2-hydroxyphenyl)-1-cyclopenten-1-yl]-2-pyridinecarboxylic acid. LC/MS t=3.05, [MH⁺] 330.4

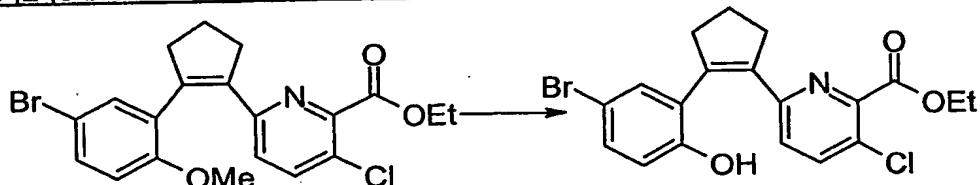
Ethyl 6-[2-(5-bromo-2-hydroxyphenyl)-1-cyclopenten-1-yl]-2-pyridinecarboxylate



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1.0M boron tribromide in dichloromethane (9.95ml, 9.95mmol) was added to a solution of ethyl 6-[2-(5-bromo-2-hydroxyphenyl)-1-cyclopenten-1-yl]-2-pyridinecarboxylate (2.0g, 4.98mmol) in dry dichloromethane (50ml) at -78°C. The reaction mixture was allowed to warm to room temperature over 4 hours. The mixture was quenched with water (50ml). The organic phase was separated, dried and evaporated to give the title compound as a yellow solid 2.0g 100%. LC/MS: Rt = 3.64 min. [M+H] = 388, 390 (1Br).

Ethyl 6-[2-(5-bromo-2-hydroxyphenyl)-1-cyclopenten-1-yl]-3-chloro-2-pyridinecarboxylate



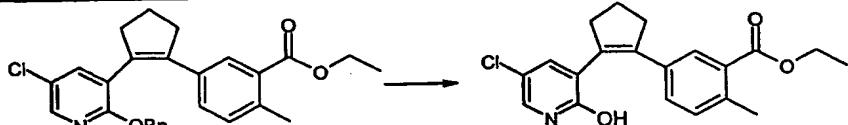
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A solution of ethyl 6-[2-[5-bromo-2-(methyloxy)phenyl]-1-cyclopenten-1-yl]-3-chloro-2-pyridinecarboxylate (501mg, 1.15mmol) in dichloromethane (5ml) was cooled to -50°C and 1M boron tribromide in dichloromethane (5ml) was added. The mixture was allowed to warm to room temperature and after 2 hours was poured onto ice and basified with 2M sodium hydroxide solution then acidified with acetic acid. The organic layer was separated, dried (magnesium sulphate), toluene (10ml) added and

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evaporated to dryness. The residue was dissolved in ethanol (25ml) and sulphuric acid (2ml) and refluxed for 5 hours then left at room temperature for 15 hours. After evaporation the residue was dissolved in ether/water, basified with potassium carbonate and the organic phase dried (magnesium sulphate), evaporated and purified by chromatography on silica eluting with ethyl acetate/iso-hexane (18:82) to give 415mg of colourless gum. LC/MS t=3.97, [MH⁺] 424.3

Ethyl 5-[2-(5-chloro-2-oxo-1,2-dihydro-3-pyridinyl)-1-cyclopenten-1-yl]-2-methylbenzoate

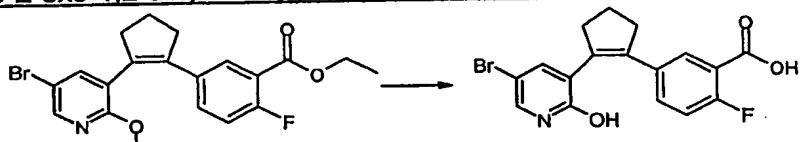


10 Ethyl 5-(2-{5-chloro-2-[(phenylmethyl)oxy]-3-pyridinyl}-1-cyclopenten-1-yl)-2-methylbenzoate (200mg, 0.447mmol) was dissolved in glacial acetic acid (0.5ml) and 45% hydrogen bromide in acetic acid (1ml) added. The mixture was stirred at room temperature for 1.5 hours. 5% sodium bicarbonate solution was added carefully, followed by diethyl ether. The aqueous layer was re-extracted with diethyl ether and the combined extracts washed with 5% sodium bicarbonate solution, dried ($MgSO_4$) and evaporated to leave the title compound (76mg). LC/MS Rt=3.51min [MH⁺] 356, 358.

15 The following intermediates were prepared by a similar route to ethyl 5-[2-(5-chloro-2-oxo-1,2-dihydro-3-pyridinyl)-1-cyclopenten-1-yl]-2-methylbenzoate from the appropriate intermediates.

	Name	Data
	Ethyl 2-fluoro-5-[2-[2-oxo-5-(trifluoromethyl)-1,2-dihydro-3-pyridinyl]-1-cyclopenten-1-yl]benzoate	LC/MS Rt=3.54min [MH ⁺] 396.
	Ethyl 6-[2-[2-oxo-5-(trifluoromethyl)-1,2-dihydro-3-pyridinyl]-1-cyclopenten-1-yl]-2-pyridinecarboxylate	LC/MS Rt=3.12min [MH ⁺] 379.

5-[2-(5-Bromo-2-oxo-1,2-dihydro-3-pyridinyl)-1-cyclopenten-1-yl]-2-fluorobenzoic acid



25 Ethyl 5-[2-[5-bromo-2-(methyloxy)-3-pyridinyl]-1-cyclopenten-1-yl]-2-fluorobenzoate (127mg, 0.302mmol), was dissolved in glacial acetic acid (1ml) and 48% aqueous hydrogen bromide (1ml) added. The mixture was heated to reflux for 45 minutes. 5% Sodium bicarbonate solution was added carefully and the mixture extracted with ethyl

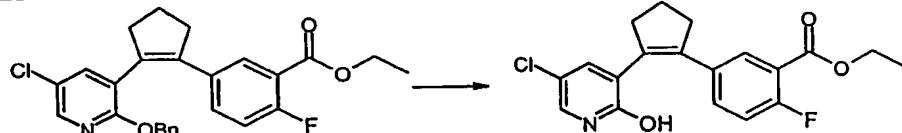
acetate. The organic layer was washed with water, dried (MgSO_4) and evaporated to give the title compound (96mg). LC/MS Rt=3.19min [MH^+] 378, 380.

The following intermediates were prepared by a similar route to 5-[2-(5-bromo-2-oxo-1,2-dihydro-3-pyridinyl)-1-cyclopenten-1-yl]-2-fluorobenzoic acid from the appropriate intermediates.

	Name	LC/MS
	2-Fluoro-5-[2-(2-oxo-1,2-dihydro-3-pyridinyl)-1-cyclopenten-1-yl]benzoic acid	Rt=2.66min [MH^+] 300.
	6-[2-(2-Oxo-1,2-dihydro-3-pyridinyl)-1-cyclopenten-1-yl]-2-pyridinecarboxylic acid	Rt=1.48min [MH^+] 283
	3-[2-(5-Bromo-2-oxo-1,2-dihydro-3-pyridinyl)-1-cyclopenten-1-yl]benzoic acid	Rt = 2.89min [MH^+] 358, 360

Ethyl 5-[2-(5-chloro-2-oxo-1,2-dihydro-3-pyridinyl)-1-cyclopenten-1-yl]-2-fluorobenzoate

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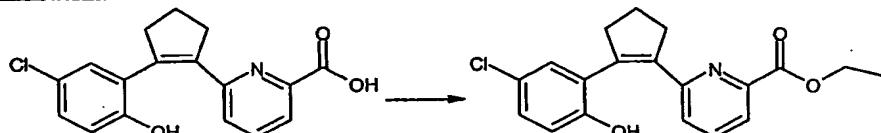
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Ethyl 5-(2-{5-chloro-2-[(phenylmethyl)oxy]-3-pyridinyl}-1-cyclopenten-1-yl)-2-fluorobenzoate (1.32g, 2.93mmol) was stirred in trifluoracetic acid (1ml) at room temperature for 20 hours and at 50°C for 12 hours. The mixture was poured carefully into 5% sodium bicarbonate solution and diethyl ether added. The organic layer was washed with 5% sodium bicarbonate solution, dried (MgSO_4) and evaporated to give the title compound as an orange oil which crystallised (1.06g).

LC/MS Rt=3.25min [MH^+] 362.5, 364.5.

Ethyl 6-[2-(5-chloro-2-hydroxyphenyl)-1-cyclopenten-1-yl]-2-pyridine carboxylate

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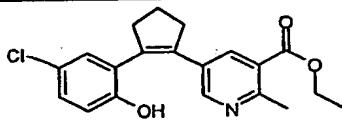
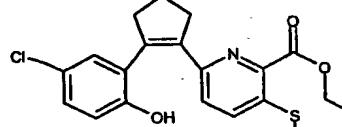
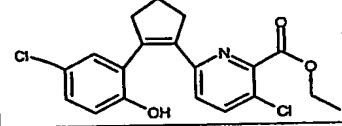
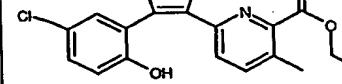
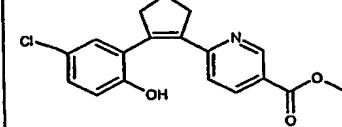
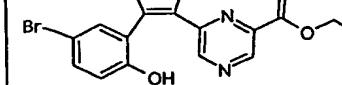
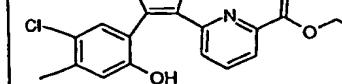
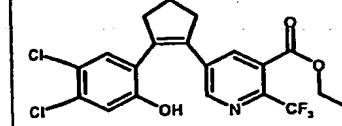


6-[2-(5-chloro-2-hydroxyphenyl)-1-cyclopenten-1-yl]-2-pyridinecarboxylic acid (2.6g, 0.0082mol) and concentrated sulphuric acid (1ml) in 100ml of ethanol were refluxed overnight. After cooling the mixture was quenched with ammonia, diluted with water and extracted with ethyl acetate (30ml x 3). The combined organic layers were washed with a

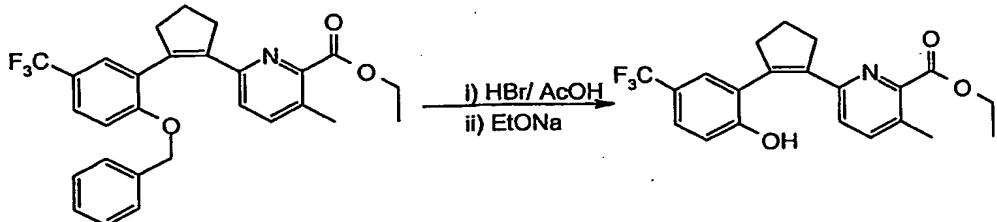
saturated solution of sodium bicarbonate, dried (magnesium sulphate) and evaporated to dryness to give the title compound as a light yellow oil (2.5g, 89%).

LC/MS: Rt 3.65 [MH⁺] 344,346 [MH-] 342,344

5 The following intermediates were prepared by a similar route to ethyl 6-[2-(5-chloro-2-hydroxyphenyl)-1-cyclopenten-1-yl]-2-pyridine carboxylate from the appropriate intermediates.

	Name	Data
	Ethyl 5-[2-(5-chloro-2-hydroxyphenyl)-1-cyclopenten-1-yl]-2-methyl-3-pyridinecarboxylate	LC/MS t=3.62, [MH ⁺] 358.4, 360.4
	Ethyl 6-[2-(5-chloro-2-hydroxyphenyl)-1-cyclopenten-1-yl]-3-(methylthio)-2-pyridinecarboxylate	LC/MS t=3.75, [MH ⁺] 390.4, 392.4
	Ethyl 3-chloro-6-[2-(5-chloro-2-hydroxyphenyl)-1-cyclopenten-1-yl]-2-pyridinecarboxylate	LC/MS t=3.93, [MH ⁺] 378.4
	Ethyl 6-[2-(5-chloro-2-hydroxyphenyl)-1-cyclopenten-1-yl]-3-methyl-2-pyridinecarboxylate	LC/MS t=3.82, [MH ⁺] 358.4, 360.4
	Ethyl 6-[2-(5-chloro-2-hydroxyphenyl)-1-cyclopenten-1-yl]-3-pyridinecarboxylate	LC/MS t=3.67, [MH ⁺] 344.3, 346.3
	Ethyl 6-[2-(5-bromo-2-hydroxyphenyl)-1-cyclopenten-1-yl]-2-pyrazinecarboxylate	LC/MS: Rt = 3.48min. [M+H] = 389, 391.
	Ethyl 6-[2-(5-chloro-2-hydroxy-4-methylphenyl)-1-cyclopenten-1-yl]-2-pyridinecarboxylate	LC/MS: Rt = 3.74 min. [M+H] = 358.
	Ethyl 5-[2-(4,5-dichloro-2-hydroxyphenyl)-1-cyclopenten-1-yl]-2-(trifluoromethyl)-3-pyridinecarboxylate	LC/MS: Rt = 3.86 min. [M+H] = 378, 380 .

Ethyl 6-{2-[2-hydroxy-5-(trifluoromethyl)phenyl]-1-cyclopenten-1-yl}-3-methyl-2-pyridinecarboxylate



A mixture of ethyl 3-methyl-6-{2-[2-[(phenylmethyl)oxy]-5-(trifluoromethyl)phenyl]-1-cyclopenten-1-yl}-2-pyridinecarboxylate (2.21 g, 4.59 mmol) dissolved in acetic acid (5 ml) and 45% hydrogen bromide in acetic acid (10 ml) was stirred at room temperature for 3 hours. The reaction mixture was diluted with diethyl ether and water and basified with potassium carbonate. The ether layer was separated, dried over magnesium sulphate and evaporated to dryness. The residue was purified using flash chromatography eluting with ethyl acetate/ iso-hexane (15%) to give 1.44 g of yellow solid. Sodium hydride (2mg) was added to the product dissolved in ethanol and left at room temperature for 12 hours. The reaction mixture was diluted with diethyl ether and water, then acidified with acetic acid. The ether layer was washed with sodium hydrogen carbonate solution, dried over magnesium sulphate and evaporated to dryness. The residue was purified using flash chromatography eluting with 20% ethyl acetate/ iso-hexane to give the title compound as a light coloured solid. 1.11 g, 62%.

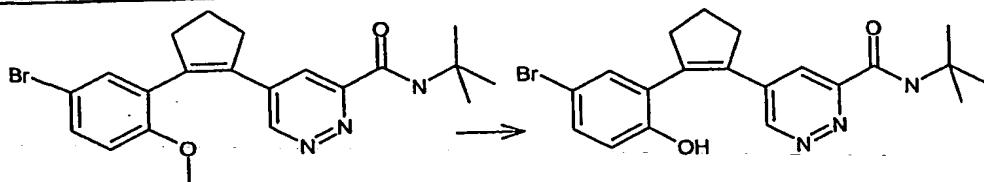
¹H NMR (CDCl₃) δ: 1.48 (3H, t), 2.08-2.15 (2H, m), 2.50 (3H, s), 2.86-3.90 (2H, m), 3.01-3.05 (2H, m), 4.45 (2H, q), 7.08 (1H, d), 7.33-7.37 (2H, m), 7.39 (1H, dd), 7.61 (1H, d).

The following intermediates were prepared by a similar route to ethyl 6-{2-[2-hydroxy-5-(trifluoromethyl)phenyl]-1-cyclopenten-1-yl}-3-methyl-2-pyridinecarboxylate from the appropriate intermediates.

	Name	Data
	Methyl 5-[2-(5-chloro-2-hydroxyphenyl)-1-cyclopenten-1-yl]-2-methyl-3-pyridinecarboxylate	LC/MS Rt=3.45, [MH ⁺] 344.3, 346.3
	Methyl 5-{2-[2-hydroxy-5-(trifluoromethyl)phenyl]-1-cyclopenten-1-yl}-2-methyl-3-pyridinecarboxylate	LC/MS Rt=3.49, [MH ⁺] 378.5
	Ethyl 3-chloro-6-{2-[2-hydroxy-5-(trifluoromethyl)phenyl]-1-cyclopenten-1-yl}-2-pyridinecarboxylate	LC/MS Rt=3.90, [MH ⁺] 412.5, 414.4

	Methyl 5-[2-(5-chloro-2-hydroxyphenyl)-1-cyclopenten-1-yl]-2-(trifluoromethyl)-3-pyridinecarboxylate	LC/MS Rt=3.75, [MH+] 398.4, 400.4
	Methyl 5-[2-[2-hydroxy-5-(trifluoromethyl)phenyl]-1-cyclopenten-1-yl]-2-(trifluoromethyl)-3-pyridinecarboxylate	LC/MS Rt = 4.02, [M H+] 446.
	Ethyl 6-[2-(5-chloro-2-hydroxyphenyl)-1-cyclopenten-1-yl]-4-(trifluoromethyl)-2-pyridinecarboxylate	LC/MS Rt = 3.45, [M H+] 412.
	Ethyl 6-[2-[2-hydroxy-5-(trifluoromethyl)phenyl]-1-cyclopenten-1-yl]-4-(trifluoromethyl)-2-pyridinecarboxylate	LC/MS Rt = 4.09, [M H+] 446.
	Ethyl 5-[2-(5-bromo-2-hydroxyphenyl)-1-cyclopenten-1-yl]-2-(trifluoromethyl)-3-pyridinecarboxylate	LC/MS Rt=3.17, [MH+] 457
	Methyl 6-[2-(5-chloro-2-hydroxyphenyl)-1-cyclopenten-1-yl]-4-pyrimidinecarboxylate	LC/MS Rt=3.07, [MH+] 331, 333
	Ethyl 2-[2-(5-chloro-2-hydroxyphenyl)-1-cyclopenten-1-yl]-3-pyridinecarboxylate	LC/MS Rt=3.26, [MH+] 344.4, 346.3

5-[2-(5-Bromo-2-hydroxyphenyl)-1-cyclopenten-1-yl]-N-(1,1-dimethylethyl)-3-pyridazinecarboxamide



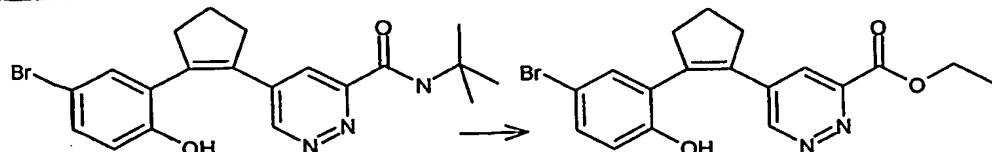
5 5-[2-[5-Bromo-2-(methyoxy)phenyl]-1-cyclopenten-1-yl]-N-(1,1-dimethylethyl)-3-pyridazinecarboxamide (5.3g, 12.3mmol) in dry dichloromethane (200ml) was cooled to -75°C under nitrogen and was treated slowly with boron tribromide (8.0ml, 84.8mmol). The

reaction mixture was then heated to reflux for 1.5 hour. The reaction mixture was then quenched in ice-water (400ml) and after stirring at room temperature for 2 hours the organic layer was dried and evaporated to a dark brown solid (6.0g).

LC/MS Rt=3.55min [MH⁺] 418, 419.

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Ethyl 5-[2-(5-bromo-2-hydroxyphenyl)-1-cyclopenten-1-yl]-3-pyridazinecarboxylate

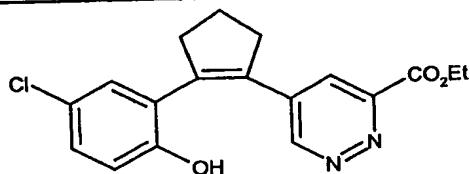


5-[2-(5-Bromo-2-hydroxyphenyl)-1-cyclopenten-1-yl]-N-(1,1-dimethylethyl)-3-pyridazinecarboxamide (6.0g, 13.95mmol) in ethanol (75ml) was treated with concentrated sulphuric acid/water (24/10ml) and refluxed for two hours. The reaction was poured into water (200ml) and extracted with ethyl acetate(3x30ml). After drying the product was purified by chromatography giving the title compound (1.8g,32% yield).

LC/MS Rt=3.2 min [MH⁺] 391, 392.

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Ethyl 5-[2-(5-chloro-2-hydroxyphenyl)-1-cyclopenten-1-yl]-3-pyridazinecarboxylate

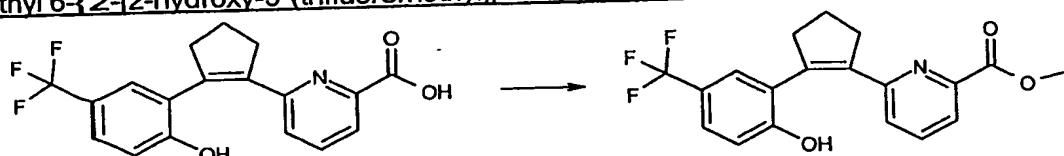


5-(2-(5-Chloro-2-[(phenylmethyl)oxy]phenyl)-1-cyclopenten-1-yl)-N-(1,1-dimethylethyl)-3-pyridazinecarboxamide (970mg, 2.1mmol) in ethanol/sulphuric acid/water 2:2:1 (20ml) was heated at 90°C for 2 hours. After cooling the solution was diluted with water/ether and the organic layer dried (magnesium sulphate) evaporated and purified by chromatography on silica eluting with ethyl acetate/iso-hexane (1:1) to give the title compound as a white solid (260mg).

LC/MS: [M+H] 345.3, 347.3, Rt=3.15min

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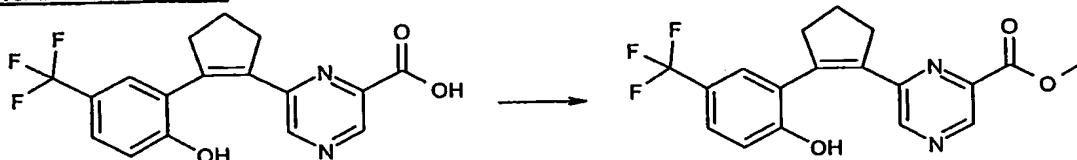
Methyl 6-[2-[2-hydroxy-5-(trifluoromethyl)phenyl]-1-cyclopenten-1-yl]-2-pyridinecarboxylate



6-{2-[2-hydroxy-5-(trifluoromethyl)phenyl]-1-cyclopenten-1-en-1-yl}pyridine-2-carboxylic acid (2.49g, 7.13mmol) was dissolved in anhydrous methanol (100ml) and cooled in an ice bath. 2M Trimethylsilyldiazomethane in hexanes (25ml) was added slowly. Bubbles of nitrogen were observed after the addition of 5ml; the addition was continued until no more bubbling was observed. The solvent was then removed *in vacuo* to yield a dark oil. This

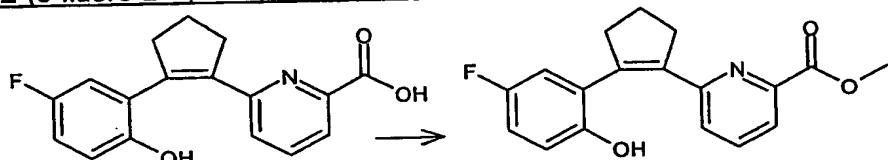
was purified by column chromatography eluting with 30% ethyl acetate/iso-hexane. This yielded the title compound as a yellow solid. LC/MS Rt = 3.47 [MH⁺] 364.

5 Methyl 6-[2-[2-hydroxy-5-(trifluoromethyl)phenyl]-1-cyclopenten-1-yl]-2-pyrazinecarboxylate



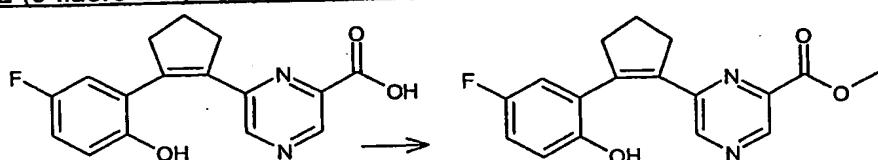
Procedure as for methyl 6-[2-(5-fluoro-2-hydroxyphenyl)-1-cyclopenten-1-yl]-2-pyridinecarboxylate. LC/MS t = 3.47, [MH⁺] 365.

10 Methyl 6-[2-(5-fluoro-2-hydroxyphenyl)-1-cyclopenten-1-yl]-2-pyridinecarboxylate



6-[2-(5-Fluoro-2-hydroxyphenyl)-1-cyclopenten-1-yl]-2-pyridinecarboxylic acid (5.0g, 16.72mmol) in methanol (200ml) and concentrated sulphuric acid (4ml) were refluxed overnight under nitrogen. The reaction mixture was then cooled and treated with .880 ammonia (8ml) and evaporated to an oil under reduced pressure. After partitioning between ethyl acetate and water, the resulting product was purified by flash chromatography with a gradient of diethyl ether/iso-hexane(10-30%) giving the title compound (3.5g,83%). LC/MS Rt=3.16min. [MH⁺] 314

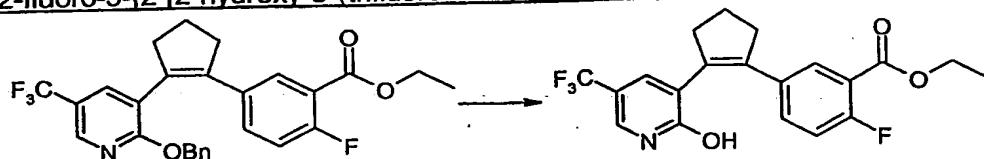
20 Methyl 6-[2-(5-fluoro-2-hydroxyphenyl)-1-cyclopenten-1-yl]-2-pyrazinecarboxylate



Procedure as for methyl 6-[2-(5-fluoro-2-hydroxyphenyl)-1-cyclopenten-1-yl]-2-pyridinecarboxylate.

LC/MS Rt = 2.98min, [MH⁺] 315.

25 Ethyl 2-fluoro-5-[2-[2-hydroxy-5-(trifluoromethyl)pyridin-3-yl]cyclopent-1-en-1-yl]benzoate

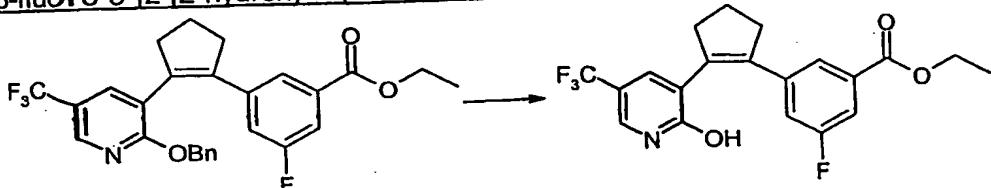


Ethyl 2-fluoro-5-[2-[2-(phenylmethoxy)-5-(trifluoromethyl)pyridin-3-yl]cyclopent-1-en-1-yl]benzoate (6.77g, 14.0mmol) was dissolved in trifluoroacetic acid (50ml). The solution

was stirred at room temperature for 36 hours. The mixture was treated with 5% aqueous sodium bicarbonate solution, and extracted with diethyl ether (*x*2). The combined extracts were dried (Na_2SO_4) and concentrated *in vacuo*. The residue was purified by flash chromatography on silica (gradient elution, 0-30% ethyl acetate/cyclohexane) to give the title compound (3.35g). LC/MS Rt=3.46min [MH^+] 396.

5

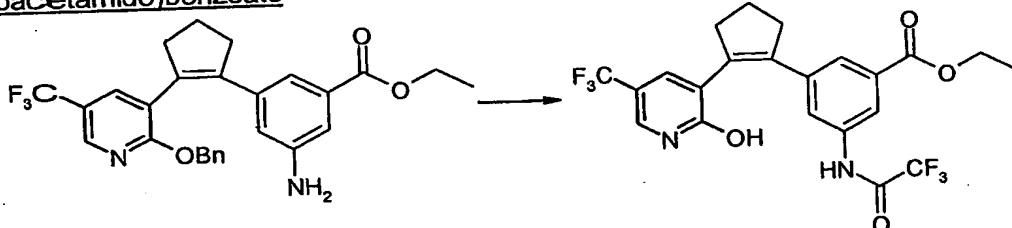
Ethyl 3-fluoro-5-{2-[2-hydroxy-5-(trifluoromethyl)pyridin-3-yl]cyclopent-1-en-1-yl}benzoate



Ethyl 3-fluoro-5-{2-[2-(phenylmethoxy)-5-(trifluoromethyl)pyridin-3-yl]cyclopent-1-en-1-yl}benzoate (7.42g, 15.3mmol) was dissolved in trifluoroacetic acid (50ml). The solution was stirred at room temperature for 18 hours. The mixture was treated with 5% aqueous sodium bicarbonate solution, and extracted with diethyl ether (*x*2). The combined extracts were dried (Na_2SO_4) and concentrated *in vacuo*. The residue was purified by flash chromatography on silica (gradient elution, 0-30% ethyl acetate/cyclohexane) to give the title compound (3.3g). LC/MS Rt=3.56min [MH^+] 396.

15

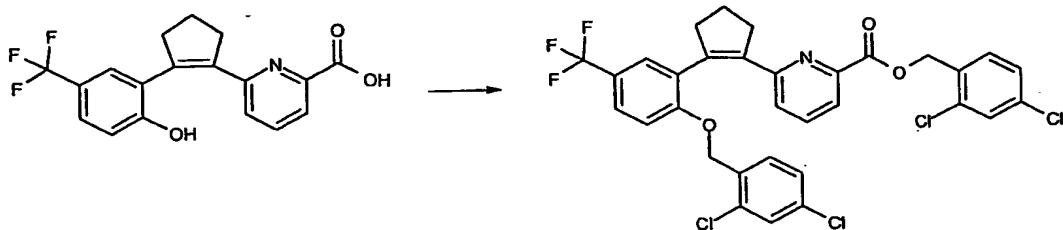
Ethyl 5-{2-[2-(hydroxy)-5-(trifluoromethyl)pyridin-3-yl]cyclopent-1-en-1-yl}-3-(trifluoroacetamido)benzoate



Ethyl 3-amino-5-{2-[2-(phenylmethoxy)-5-(trifluoromethyl)pyridin-3-yl]cyclopent-1-en-1-yl}benzoate (4.5g, 7.79mmol) was dissolved in trifluoroacetic acid (50ml) and stirred at room temperature for 20 hours. The mixture was neutralised with 5% aqueous sodium hydrogen carbonate, and extracted with water. The organic extracts were washed with further water, dried (Na_2SO_4), and concentrated *in vacuo*. The residue was purified by flash chromatography on silica (gradient elution, 0-65% ethyl acetate/cyclohexane) to give the required product (1.99g). LC/MS Rt=3.52min [MH^+] 489.

25

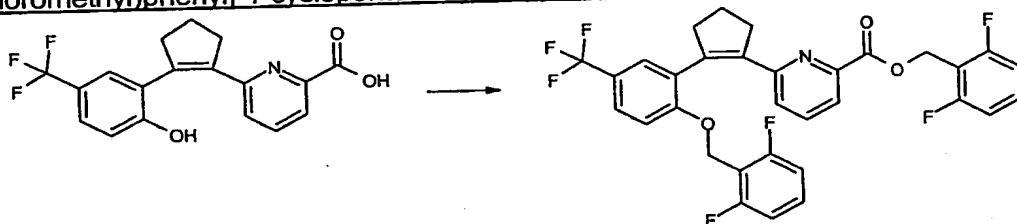
(2,4-Dichlorophenyl)methyl 6-{2-[2-[(2,4-dichlorophenyl)methyl]oxy}-5-(trifluoromethyl)phenyl]-1-cyclopenten-1-yl}-2-pyridinecarboxylate



6-{2-[2-Hydroxy-5-(trifluoromethyl)phenyl]cyclopent-1-en-1-yl}-pyridine-2-carboxylic acid (0.067g, 0.19mmol), potassium carbonate (0.079g, 0.57mmol), 2,4-dichlorobenzyl bromide (0.082g, 0.42mmol) and DMF (2ml) were heated at 55°C for 3 hours under a nitrogen atmosphere. After cooling the reaction was diluted with ethyl acetate and washed with water (x2). The aqueous layers were washed with ethyl acetate (x2). The combined organic layers were then washed with brine, dried over MgSO₄, filtered and concentrated in vacuo to give a dark oil. This was purified by column chromatography eluting with 10% ethyl acetate/isohexane to yield the title compound as a brown oil (0.095g, 74%).

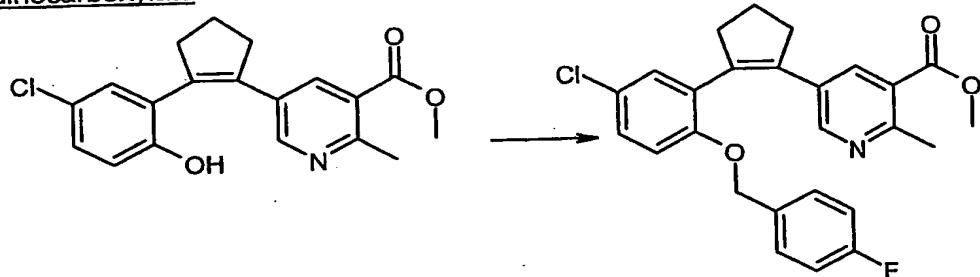
LC/MS t = 4.97, [MH⁺] 668

Methyl 6-{2-[2-[(2,6-difluorophenyl)methyl]oxy]-5-(trifluoromethyl)phenyl}-1-cyclopenten-1-yl}-2-pyridinecarboxylate



Procedure as for (2,4-dichlorophenyl)methyl 6-{2-[2-[(2,4-dichlorophenyl)methyl]oxy]-5-(trifluoromethyl)phenyl}-1-cyclopenten-1-yl}-2-pyridinecarboxylate.
LC/MS t = 4.34, [MH⁺] 602

Methyl 5-[2-(5-chloro-2-[(4-fluorophenyl)methyl]oxy)phenyl]-1-cyclopenten-1-yl]-2-methyl-3-pyridinecarboxylate

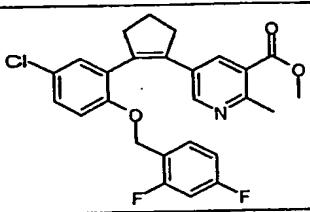
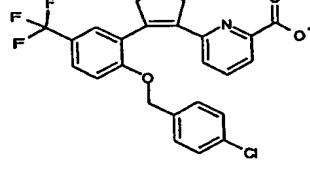
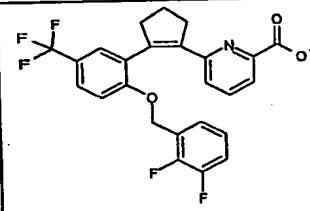
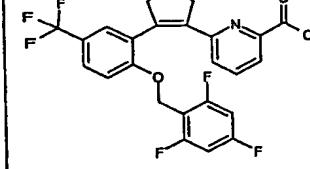
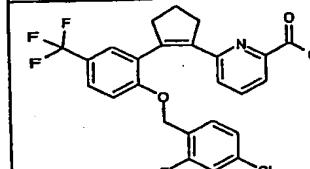


A mixture of methyl 5-[2-(5-chloro-2-hydroxyphenyl)-1-cyclopenten-1-yl]-2-methyl-3-pyridinecarboxylate (150mg, 0.44mmol), 4-fluorobenzyl bromide (95mg, 0.50mmol) and potassium carbonate (138mg, 1mmol) in acetone (5ml) was stirred and refluxed for 3

hours then cooled, filtered, evaporated and purified by chromatography on silica eluting with ethyl acetate/iso-hexane (15:85) to give a colourless gum (191mg).

LC/MS t=4.07, [MH⁺] 452.3

5 The following intermediates were prepared by a similar route to methyl 5-[2-(5-chloro-2-[(4-fluorophenyl)methyl]oxy)phenyl]-1-cyclopenten-1-yl]-2-methyl-3-pyridinecarboxylate from the appropriate intermediates.

	Name	LC/MS
	Methyl 5-[2-(5-chloro-2-[(2,4-difluorophenyl)methyl]oxy)phenyl]-1-cyclopenten-1-yl]-2-methyl-3-pyridinecarboxylate	Rt=4.09, [MH ⁺] 470.4, 472.3
	Methyl 6-{2-[2-[(4-chlorophenyl)methyl]oxy]-5-(trifluoromethyl)phenyl}-1-cyclopenten-1-yl]-2-pyridinecarboxylate	Rt = 4.16, [MH ⁺] 488
	Methyl 6-{2-[2-[(2,3-difluorophenyl)methyl]oxy]-5-(trifluoromethyl)phenyl}-1-cyclopenten-1-yl]-2-pyridinecarboxylate	Rt = 4.08 [MH ⁺] 490
	Methyl 6-[2-(5-(trifluoromethyl)-2-[(2,4,6-trifluorophenyl)methyl]oxy)phenyl]-1-cyclopenten-1-yl]-2-pyridinecarboxylate	Rt = 4.02, [MH ⁺] 508
	Methyl 6-{2-[2-[(4-chloro-2-fluorophenyl)methyl]oxy]-5-(trifluoromethyl)phenyl}-1-cyclopenten-1-yl]-2-pyridinecarboxylate	Rt = 4.20, [MH ⁺] 506

	Methyl 6-{2-[2-[(2-chlorophenyl)methyl]oxy]-5-(trifluoromethyl)phenyl}-1-cyclopenten-1-yl}-2-pyridinecarboxylate	Rt = 4.19, [MH ⁺] 488
	Methyl 6-{2-[2-[(4-bromophenyl)methyl]oxy]-5-(trifluoromethyl)phenyl}-1-cyclopenten-1-yl}-2-pyridinecarboxylate	Rt = 4.22, [MH ⁺] 532, 534
	Methyl 6-{2-[2-[(4-bromo-2-fluorophenyl)methyl]oxy]-5-(trifluoromethyl)phenyl}-1-cyclopenten-1-yl}-2-pyridinecarboxylate	Rt = 4.24, [MH ⁺] 550, 552
	Methyl 6-{2-[2-[(2-chloro-4-fluorophenyl)methyl]oxy]-5-(trifluoromethyl)phenyl}-1-cyclopenten-1-yl}-2-pyridinecarboxylate	Rt = 4.21, [MH ⁺] 506
	Methyl 6-{2-[2-[(2-chloro-6-fluorophenyl)methyl]oxy]-5-(trifluoromethyl)phenyl}-1-cyclopenten-1-yl}-2-pyridinecarboxylate	Rt = 4.09, [MH ⁺] 506
	Methyl 6-[2-(5-(trifluoromethyl)-2-[(2,3,6-trifluorophenyl)methyl]oxy)phenyl]-1-cyclopenten-1-yl}-2-pyridinecarboxylate	Rt = 3.99, [MH ⁺] 508

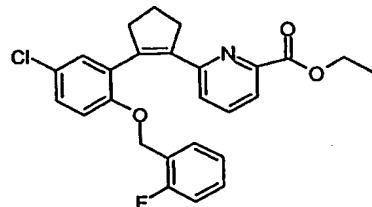
	Methyl 6-{2-[2-[(2-bromophenyl)methyl]oxy]-5-(trifluoromethyl)phenyl}-1-cyclopenten-1-yl}-2-pyridinecarboxylate	Rt = 4.22, [MH ⁺] 532, 534
	Methyl 6-{2-[2-[(4-fluorophenyl)methyl]oxy]-5-(trifluoromethyl)phenyl}-1-cyclopenten-1-yl}-2-pyridinecarboxylate	Rt = 3.92, [MH ⁺] 473
	Methyl 6-{2-[2-[(2,4-difluorophenyl)methyl]oxy]-5-(trifluoromethyl)phenyl}-1-cyclopenten-1-yl}-2-pyridinecarboxylate	Rt = 3.95, [MH ⁺] 491
	Methyl 6-{2-[2-[(4-chlorophenyl)methyl]oxy]-5-(trifluoromethyl)phenyl}-1-cyclopenten-1-yl}-2-pyridinecarboxylate	Rt = 4.21, [MH ⁺] 489
	Methyl 6-{2-[2-[(2-fluorophenyl)methyl]oxy]-5-(trifluoromethyl)phenyl}-1-cyclopenten-1-yl}-2-pyridinecarboxylate	Rt = 3.95, [MH ⁺] 473
	Methyl 6-{2-[2-[(4-bromophenyl)methyl]oxy]-5-(trifluoromethyl)phenyl}-1-cyclopenten-1-yl}-2-pyridinecarboxylate	Rt = 4.15, [MH ⁺] 533, 535
	Methyl 6-{2-[2-[(4-bromo-2-fluorophenyl)methyl]oxy]-5-(trifluoromethyl)phenyl}-1-cyclopenten-1-yl}-2-pyridinecarboxylate	Rt = 4.26, [MH ⁺] 551, 553

	Methyl 6-{2-[2-[(2-chloro-4-fluorophenyl)methyl]oxy}-5-(trifluoromethyl)phenyl]-1-cyclopenten-1-yl}-2-pyridinecarboxylate	Rt = 4.23, [MH ⁺] 507
	Methyl 5-{2-[2-[(4-fluorophenyl)methyl]oxy}-5-(trifluoromethyl)phenyl]-1-cyclopenten-1-yl}-2-methyl-3-pyridinecarboxylate	Rt=3.98, [MH ⁺] 486.5
	Methyl 5-{2-[2-[(2,4-difluorophenyl)methyl]oxy}-5-(trifluoromethyl)phenyl]-1-cyclopenten-1-yl}-2-methyl-3-pyridinecarboxylate	Rt=4.03 [MH ⁺] 504.4
	Methyl 5-{2-[2-[(2,4,6-trifluorophenyl)methyl]oxy}-5-(trifluoromethyl)phenyl]-1-cyclopenten-1-yl}-2-methyl-3-pyridinecarboxylate	Rt=4.06 [MH ⁺] 522.4
	Methyl 5-{2-[2-[(2-chloro-4-fluorophenyl)methyl]oxy}-5-(trifluoromethyl)phenyl]-1-cyclopenten-1-yl}-2-methyl-3-pyridinecarboxylate	Rt=4.22 [MH ⁺] 520.4, 522.4
	Methyl 5-{2-[2-[(4-chloro-2-fluorophenyl)methyl]oxy}-5-(trifluoromethyl)phenyl]-1-cyclopenten-1-yl}-2-methyl-3-pyridinecarboxylate	Rt=4.23 [MH ⁺] 520.4, 522.4
	Ethyl 5-{2-[2-[(2-fluorophenyl)methyl]oxy}-5-(trifluoromethyl)phenyl]-1-cyclopenten-1-yl}-2-methyl-3-pyridinecarboxylate	Rt=4.41 [MH ⁺] 500.4

	Ethyl 5-[2-[2-[(2,4,5-trifluorophenyl)methyl]oxy]-5-(trifluoromethyl)phenyl]-1-cyclopenten-1-yl]-2-methyl-3-pyridinecarboxylate	Rt=4.57 [MH+] 536.4
	Methyl 5-[2-(5-chloro-2-[(2-fluorophenyl)methyl]oxy)phenyl]-1-cyclopenten-1-yl]-2-(trifluoromethyl)-3-pyridinecarboxylate	Rt=3.95, [MH+] 506.4
	Methyl 5-[2-(5-chloro-2-[(4-fluorophenyl)methyl]oxy)phenyl]-1-cyclopenten-1-yl]-2-(trifluoromethyl)-3-pyridinecarboxylate	Rt=3.96 [MH+] 506.4
	Methyl 5-[2-(5-chloro-2-[(2,4-difluorophenyl)methyl]oxy)phenyl]-1-cyclopenten-1-yl]-2-(trifluoromethyl)-3-pyridinecarboxylate	Rt=3.95 [MH+] 524.4
	Methyl 5-[2-(5-chloro-2-[(2-chloro-4-fluorophenyl)methyl]oxy)phenyl]-1-cyclopenten-1-yl]-2-(trifluoromethyl)-3-pyridinecarboxylate	Rt=4.06 [MH+] 540.3
	Methyl 5-[2-(5-chloro-2-[(2,6-difluorophenyl)methyl]oxy)phenyl]-1-cyclopenten-1-yl]-2-(trifluoromethyl)-3-pyridinecarboxylate	Rt=3.93 [MH+] 524.4
	Methyl 5-[2-(5-chloro-2-[(4-chloro-2-fluorophenyl)methyl]oxy)phenyl]-1-cyclopenten-1-yl]-2-(trifluoromethyl)-3-pyridinecarboxylate	Rt=4.11 [MH+] 540.3
	Methyl 5-[2-(5-chloro-2-[(2,4,6-trifluorophenyl)methyl]oxy)phenyl]-1-cyclopenten-1-yl]-2-(trifluoromethyl)-3-pyridinecarboxylate	Rt=4.02 [MH+] 542.3
	Methyl 5-[2-(5-chloro-2-[(2,3,4-trifluorophenyl)methyl]oxy)phenyl]-1-cyclopenten-1-yl]-2-(trifluoromethyl)-3-pyridinecarboxylate	Rt=4.01 [MH+] 542.3

	Methyl 5-[2-(5-chloro-2-{[(2,4,5-trifluorophenyl)methyl]oxy}phenyl)-1-cyclopenten-1-yl]-2-(trifluoromethyl)-3-pyridinecarboxylate	Rt=4.04 [MH ⁺] 542.3
	Methyl 6-[2-(5-chloro-2-{[(2,4-difluorophenyl)methyl]oxy}phenyl)-1-cyclopenten-1-yl]-4-pyridinecarboxylate	Rt=4.10 [MH ⁺] 457, 459

Ethyl 6-[2-(5-chloro-2-{[(2-fluorophenyl)methyl]oxy}phenyl)-1-cyclopenten-1-yl]-2-pyridinecarboxylate

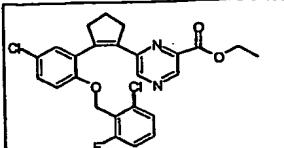
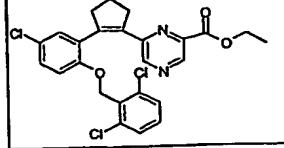
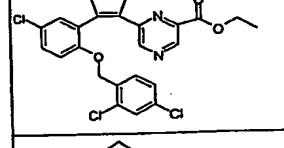
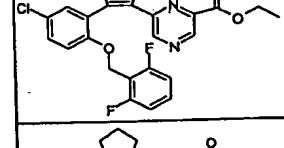
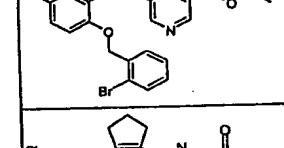
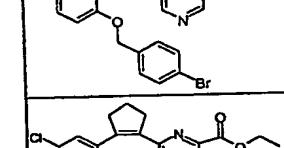
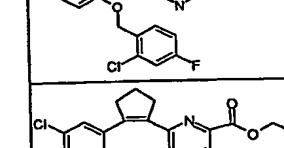
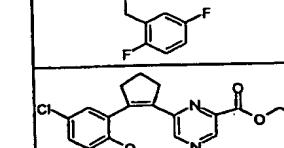
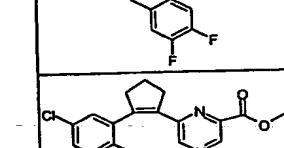
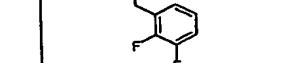


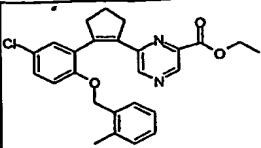
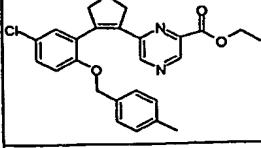
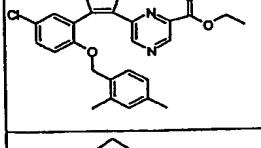
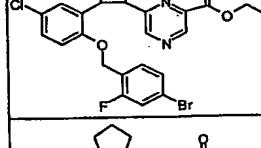
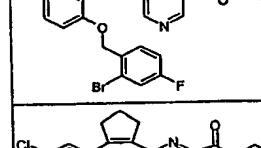
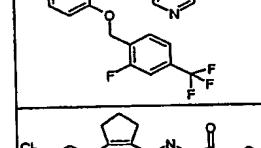
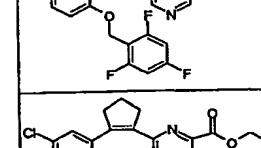
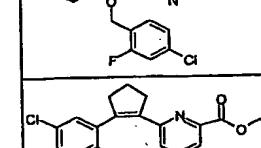
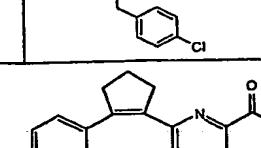
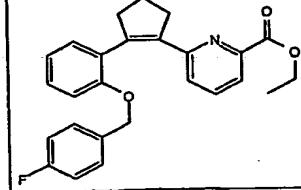
5 Ethyl 6-[2-(5-chloro-2-hydroxyphenyl)-1-cyclopenten-1-yl]-2-pyridinecarboxylate (100mg, 0.29 mmol), 2-fluorobenzyl bromide (0.035ml, 0.32 mmol) and potassium carbonate (100mg, 0.73 mmol) in acetone (3ml) were refluxed overnight under nitrogen . The reaction mixture was then filtered through hiflo and evaporated to give the title compound. LC/MS: Rt=4.1 [MH⁺] 452,455

10 The following intermediates were prepared by a similar route to ethyl 6-[2-(5-chloro-2-{[(2-fluorophenyl)methyl]oxy}phenyl)-1-cyclopenten-1-yl]-2-pyridinecarboxylate from the appropriate intermediates.

	Name	LC/MS
	Ethyl 6-[2-(5-chloro-2-{[(2-chloro-6-fluorophenyl)methyl]oxy}phenyl)-1-cyclopenten-1-yl]-2-pyridinecarboxylate	Rt = 4.20, [MH ⁺] 486,489
	Ethyl 6-[2-(5-chloro-2-{[(2-chlorophenyl)methyl]oxy}phenyl)-1-cyclopenten-1-yl]-2-pyridinecarboxylate	Rt = 4.28, [MH ⁺] 468,471
	Ethyl 6-[2-(5-chloro-2-{[(2-methylphenyl)methyl]oxy}phenyl)-1-cyclopenten-1-yl]-2-pyridinecarboxylate	Rt = 3.99, [MH ⁺] 448,451

	Ethyl 6-[2-(5-chloro-2-[(2,6-dichlorophenyl)methyl]oxy)phenyl]-1-cyclopenten-1-yl]-2-pyridinecarboxylate	Rt = 4.08, [MH ⁺] 504,506
	Ethyl 6-[2-(5-chloro-2-[(2,4-dimethylphenyl)methyl]oxy)phenyl]-1-cyclopenten-1-yl]-2-pyridinecarboxylate	Rt = 4.09, [MH ⁺] 462,464
	Ethyl 6-[2-(5-chloro-2-[(2,3,6-trifluorophenyl)methyl]oxy)phenyl]-1-cyclopenten-1-yl]-2-pyridinecarboxylate	Rt = 4.11, [MH ⁺] 488,490
	Ethyl 6-[2-(2-[(4-bromo-2-fluorophenyl)methyl]oxy)-5-chlorophenyl]-1-cyclopenten-1-yl]-2-pyridinecarboxylate	Rt = 4.11, [MH ⁺] 532,534
	Ethyl 6-[2-(5-chloro-2-[(2,5-difluorophenyl)methyl]oxy)phenyl]-1-cyclopenten-1-yl]-2-pyridinecarboxylate	Rt = 3.95, [MH ⁺] 470,473
	Ethyl 6-[2-(2-[(2-bromophenyl)methyl]oxy)-5-chlorophenyl]-1-cyclopenten-1-yl]-2-pyridinecarboxylate	Rt = 4.32, [MH ⁺] 514,516
	Ethyl 6-[2-(5-chloro-2-[(2,4-dichlorophenyl)methyl]oxy)phenyl]-1-cyclopenten-1-yl]-2-pyridinecarboxylate	Rt = 4.45, [MH ⁺] 504,506
	Ethyl 6-[2-(2-[(2-bromo-4-fluorophenyl)methyl]oxy)-5-chlorophenyl]-1-cyclopenten-1-yl]-2-pyridinecarboxylate	Rt = 4.33, [MH ⁺] 532,534
	Ethyl 6-[2-(5-chloro-2-[(2-fluorophenyl)methyl]oxy)phenyl]-1-cyclopenten-1-yl]-2-pyrazinecarboxylate	Rt = 3.81, [MH ⁺] 453,456
	Ethyl 6-[2-(5-chloro-2-[(2-chlorophenyl)methyl]oxy)phenyl]-1-cyclopenten-1-yl]-2-pyrazinecarboxylate	Rt = 3.96, [MH ⁺] 469.472

	Ethyl 6-[2-(5-chloro-2-{[(2-chloro-6-fluorophenyl)methyl]oxy}phenyl)-1-cyclopenten-1-yl]-2-pyrazinecarboxylate	Rt = 3.88, [MH ⁺] 487,490
	Ethyl 6-[2-(5-chloro-2-{[(2,6-dichlorophenyl)methyl]oxy}phenyl)-1-cyclopenten-1-yl]-2-pyrazinecarboxylate	Rt = 4.19, [MH ⁺] 505,507
	Ethyl 6-[2-(5-chloro-2-{[(2,4-dichlorophenyl)methyl]oxy}phenyl)-1-cyclopenten-1-yl]-2-pyrazinecarboxylate	Rt = 4.32, [MH ⁺] 505,507
	Ethyl 6-[2-(5-chloro-2-{[(2,6-difluorophenyl)methyl]oxy}phenyl)-1-cyclopenten-1-yl]-2-pyrazinecarboxylate	Rt = 3.97, [MH ⁺] 473,474
	Ethyl 6-[2-(2-{[(2-bromophenyl)methyl]oxy}-5-chlorophenyl)-1-cyclopenten-1-yl]-2-pyrazinecarboxylate	Rt = 3.99, [MH ⁺] 515,517
	Ethyl 6-[2-(2-{[(4-bromophenyl)methyl]oxy}-5-chlorophenyl)-1-cyclopenten-1-yl]-2-pyrazinecarboxylate	Rt = 3.98, [MH ⁺] 515,517
	Ethyl 6-[2-(5-chloro-2-{[(2-chloro-4-fluorophenyl)methyl]oxy}phenyl)-1-cyclopenten-1-yl]-2-pyrazinecarboxylate	Rt = 3.97, [MH ⁺] 487,490
	Ethyl 6-[2-(5-chloro-2-{[(2,5-difluorophenyl)methyl]oxy}phenyl)-1-cyclopenten-1-yl]-2-pyrazinecarboxylate	Rt = 3.83, [MH ⁺] 471,473
	Ethyl 6-[2-(5-chloro-2-{[(3,4-difluorophenyl)methyl]oxy}phenyl)-1-cyclopenten-1-yl]-2-pyrazinecarboxylate	Rt = 3.84, [MH ⁺] 471,473
	Ethyl 6-[2-(5-chloro-2-{[(2,3-difluorophenyl)methyl]oxy}phenyl)-1-cyclopenten-1-yl]-2-pyrazinecarboxylate	Rt = 3.82, [MH ⁺] 471,473

	Ethyl 6-[2-(5-chloro-2-[(2-methylphenyl)methoxy]phenyl)-1-cyclopenten-1-yl]-2-pyrazinecarboxylate	Rt = 4.34, [MH+] 449
	Ethyl 6-[2-(5-chloro-2-[(4-methylphenyl)methoxy]phenyl)-1-cyclopenten-1-yl]-2-pyrazinecarboxylate	Rt = 4.37, [MH+] 449, 451
	Ethyl 6-[2-(5-chloro-2-[(2,4-dimethylphenyl)methoxy]phenyl)-1-cyclopenten-1-yl]-2-pyrazinecarboxylate	Rt = 4.48, [MH+] 463
	Ethyl 6-[2-(2-[(4-bromo-2-fluorophenyl)methoxy]-5-chlorophenyl)-1-cyclopenten-1-yl]-2-pyrazinecarboxylate	Rt = 4.47, [MH+] 533, 535
	Ethyl 6-[2-(2-[(2-bromo-4-fluorophenyl)methoxy]-5-chlorophenyl)-1-cyclopenten-1-yl]-2-pyrazinecarboxylate	Rt = 4.48, [MH+] 533 [MH-] 531
	Ethyl 6-[2-(5-chloro-2-[(2-fluoro-4-(trifluoromethyl)phenyl)methoxy]phenyl)-1-cyclopenten-1-yl]-2-pyrazinecarboxylate	Rt = 4.46, [MH+] 521, 523
	Ethyl 6-[2-(5-chloro-2-[(2,4,6-trifluorophenyl)methoxy]phenyl)-1-cyclopenten-1-yl]-2-pyrazinecarboxylate	Rt = 4.23, [MH+] 489, 491
	Ethyl 6-[2-(5-chloro-2-[(4-chloro-2-fluorophenyl)methoxy]phenyl)-1-cyclopenten-1-yl]-2-pyrazinecarboxylate	Rt = 4.23, [MH+] 487
	Ethyl 6-[2-(5-chloro-2-[(4-chlorophenyl)methoxy]phenyl)-1-cyclopenten-1-yl]-2-pyrazinecarboxylate	Rt = 4.23, [MH+] 469, 471
	Ethyl 6-[2-(2-[(4-fluorophenyl)methoxy]phenyl)-1-cyclopenten-1-yl]-2-pyridinecarboxylate	Rt = 3.99 min, [M+H] - 418.

	Ethyl 6-[2-(2-[(4-chlorophenyl)methyl]oxy)phenyl]-1-cyclopenten-1-yl]-2-pyridinecarboxylate	Rt = 4.16 min, [M+H] 434.
	Ethyl 6-[2-(2-[(4-bromophenyl)methyl]oxy)phenyl]-1-cyclopenten-1-yl]-2-pyridinecarboxylate	Rt = 4.21 min, [M+H] 480.
	Ethyl 6-[2-(2-[(4-methylphenyl)methyl]oxy)phenyl]-1-cyclopenten-1-yl]-2-pyridinecarboxylate	Rt = 4.11 min, [M+H] 414.
	Ethyl 6-[2-{2-[(4-(trifluoromethyl)phenyl)methyl]oxy}phenyl]-1-cyclopenten-1-yl]-2-pyridinecarboxylate	Rt = 4.17 min, [M+H] 486.
	Ethyl 6-[2-(2-[(2-fluorophenyl)methyl]oxy)phenyl]-1-cyclopenten-1-yl]-2-pyridinecarboxylate	Rt = 3.99 min, [M+H] 418.
	Ethyl 6-[2-(2-[(2-chlorophenyl)methyl]oxy)phenyl]-1-cyclopenten-1-yl]-2-pyridinecarboxylate	Rt = 4.18 min, [M+H] 434.
	Ethyl 6-[2-(2-[(2-bromophenyl)methyl]oxy)phenyl]-1-cyclopenten-1-yl]-2-pyridinecarboxylate	Rt = 4.18 min, [M+H] 480.

	Ethyl 6-[2-(2-[(2-methylphenyl)methyl]oxy)phenyl]-1-cyclopenten-1-yl]-2-pyridinecarboxylate 414.	Rt = 4.06 min, [M+H]
	Ethyl 6-[2-(2-[(4-chloro-2-fluorophenyl)methyl]oxy)phenyl]-1-cyclopenten-1-yl]-2-pyridinecarboxylate 452.	Rt = 4.18 min, [M+H]
	Ethyl 6-[2-(2-[(4-bromo-2-fluorophenyl)methyl]oxy)phenyl]-1-cyclopenten-1-yl]-2-pyridinecarboxylate 498.	Rt = 4.21 min, [M+H]
	Ethyl 6-[2-[2-({[2-fluoro-4-(trifluoromethyl)phenyl]methyl}oxy)phenyl]-1-cyclopenten-1-yl]-2-pyridinecarboxylate 486.	Rt = 4.22 min, [M+H]
	Ethyl 6-[2-(2-[(2-chloro-4-fluorophenyl)methyl]oxy)phenyl]-1-cyclopenten-1-yl]-2-pyridinecarboxylate 452.	Rt = 4.21 min, [M+H]
	Ethyl 6-[2-(2-[(2,4-dichlorophenyl)methyl]oxy)phenyl]-1-cyclopenten-1-yl]-2-pyridinecarboxylate 468.	Rt = 4.43 min, [M+H]
	Ethyl 6-[2-(2-[(2-bromo-4-fluorophenyl)methyl]oxy)phenyl]-1-cyclopenten-1-yl]-2-pyridinecarboxylate 498.	Rt = 4.26 min, [M+H]
	Ethyl 6-[2-(2-[(2,4-dimethylphenyl)methyl]oxy)phenyl]-1-cyclopenten-1-yl]-2-pyridinecarboxylate 428.	Rt = 4.22 min, [M+H]

	Ethyl 6-[2-(2-((2,4-bis(trifluoromethyl)phenyl)methyl)oxy)phenyl]-1-cyclopenten-1-yl]-2-pyridinecarboxylate Rt = 4.43 min, [M+H] 536.	
	Ethyl 6-[2-(2-((3,4-difluorophenyl)methyl)oxy)phenyl]-1-cyclopenten-1-yl]-2-pyridinecarboxylate Rt = 4.03 min, [M+H] 436.	
	Ethyl 6-[2-(2-((2,4,6-trifluorophenyl)methyl)oxy)phenyl]-1-cyclopenten-1-yl]-2-pyridinecarboxylate Rt = 3.98 min, [M+H] 454.	
	Ethyl 6-[2-(2-((2,4,6-trimethylphenyl)methyl)oxy)phenyl]-1-cyclopenten-1-yl]-2-pyridinecarboxylate Rt = 4.31 min, [M+H] 442.	
	Ethyl 6-[2-(2-((2,3,6-trifluorophenyl)methyl)oxy)phenyl]-1-cyclopenten-1-yl]-2-pyridinecarboxylate Rt = 3.95 min, [M+H] 454.	
	Ethyl 6-[2-(2-((2,4,5-trifluorophenyl)methyl)oxy)phenyl]-1-cyclopenten-1-yl]-2-pyridinecarboxylate Rt = 4.08 min, [M+H] 454.	
	Ethyl 6-[2-(2-((3,4,5-trifluorophenyl)methyl)oxy)phenyl]-1-cyclopenten-1-yl]-2-pyridinecarboxylate Rt = 4.12 min, [M+H] 454.	

	Ethyl 6-(2-{[(phenylmethyl)oxy]phenyl}-1-cyclopenten-1-yl)-2-pyrazinecarboxylate	Rt = 3.83 min, [M+H] 401.
	Ethyl 6-[2-{[(4-fluorophenyl)methyl]oxy}phenyl]-1-cyclopenten-1-yl)-2-pyrazinecarboxylate	Rt = 3.86 min, [M+H] 419.
	Ethyl 6-[2-{[(4-chlorophenyl)methyl]oxy}phenyl]-1-cyclopenten-1-yl)-2-pyrazinecarboxylate	Rt = 3.75 min, [M+H] 437.
	Ethyl 6-[2-{[(2,4-difluorophenyl)methyl]oxy}phenyl]-1-cyclopenten-1-yl)-2-pyrazinecarboxylate	Rt = 4.03 min, [M+H] 435.
	Ethyl 6-[2-{[(4-chloro-2-fluorophenyl)methyl]oxy}phenyl]-1-cyclopenten-1-yl)-2-pyrazinecarboxylate	Rt = 4.07 min, [M+H] 453.
	Ethyl 6-[2-{[(2,4-dichlorophenyl)methyl]oxy}phenyl]-1-cyclopenten-1-yl)-2-pyrazinecarboxylate	Rt = 4.21 min, [M+H] 469.
	Ethyl 6-[2-{[(2,5-difluorophenyl)methyl]oxy}phenyl]-1-cyclopenten-1-yl)-2-pyrazinecarboxylate	Rt = 3.89 min, [M+H] 437.

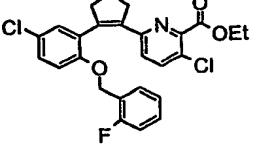
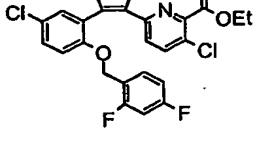
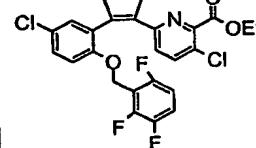
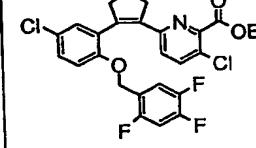
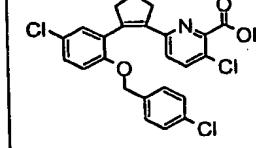
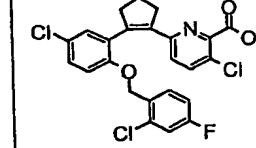
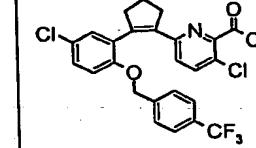
	Ethyl 6-[2-(2-{[(2-fluorophenyl)methyl]oxy}phenyl)-1-cyclopenten-1-yl]-2-pyrazinecarboxylate Rt = 3.85 min, [M+H] 419.
	Ethyl 6-[2-(2-{[(2,4,6-trifluorophenyl)methyl]oxy}phenyl)-1-cyclopenten-1-yl]-2-pyrazinecarboxylate Rt = 3.84 min, [M+H] 455.
	Ethyl 5-(2-{[5-chloro-2-[(phenylmethyl)oxy]phenyl}-1-cyclopenten-1-yl)-2-ethyl-3-pyridinecarboxylate Rt = 4.35 min, [M+H] 462.
	Ethyl 5-[2-(5-chloro-2-{[(4-fluorophenyl)methyl]oxy}phenyl)-1-cyclopenten-1-yl]-2-ethyl-3-pyridinecarboxylate Rt = 4.34 min, [M+H] 480.
	Ethyl 5-[2-(5-chloro-2-{[(4-chlorophenyl)methyl]oxy}phenyl)-1-cyclopenten-1-yl]-2-ethyl-3-pyridinecarboxylate Rt = 4.51 min, [M+H] 496.
	Ethyl 5-[2-{[5-chloro-2-({[4-(trifluoromethyl)phenyl)methyl]oxy}phenyl)-1-cyclopenten-1-yl]-2-ethyl-3-pyridinecarboxylate Rt = 4.51 min, [M+H] 530.
	Ethyl 5-[2-(5-chloro-2-{[(2-fluorophenyl)methyl]oxy}phenyl)-1-cyclopenten-1-yl]-2-ethyl-3-pyridinecarboxylate Rt = 4.35 min, [M+H] 480.
	Ethyl 5-[2-(5-chloro-2-{[(2,4-difluorophenyl)methyl]oxy}phenyl)-1-cyclopenten-1-yl]-2-ethyl-3-pyridinecarboxylate Rt = 4.37 min, [M+H] 498.

	Ethyl 5-[2-(5-chloro-2-[(2,6-difluorophenyl)methyl]oxy)phenyl]-1-cyclopenten-1-yl]-2-ethyl-3-pyridinecarboxylate	Rt = 4.29 min, [M+H] 498.
	Ethyl 5-[2-(5-chloro-2-[(2-chloro-4-fluorophenyl)methyl]oxy)phenyl]-1-cyclopenten-1-yl]-2-ethyl-3-pyridinecarboxylate	Rt = 4.54 min, [M+H] 514.
	Ethyl 5-[2-(5-chloro-2-[(2,4,5-trifluorophenyl)methyl]oxy)phenyl]-1-cyclopenten-1-yl]-2-ethyl-3-pyridinecarboxylate	Rt = 4.40 min, [M+H] 516.
	Ethyl 5-[2-(5-chloro-2-[(2,4,6-trifluorophenyl)methyl]oxy)phenyl]-1-cyclopenten-1-yl]-2-ethyl-3-pyridinecarboxylate	Rt = 4.33 min, [M+H] 516.
	Ethyl 3-methyl-6-{2-[2-[(phenylmethyl)oxy]-5-(trifluoromethyl)phenyl]-1-cyclopenten-1-yl}-2-pyridinecarboxylate	Rt = 4.35 min, [M+H] 482.
	Ethyl 6-{2-[2-[(4-fluorophenyl)methyl]oxy]-5-(trifluoromethyl)phenyl}-1-cyclopenten-1-yl]-3-methyl-2-pyridinecarboxylate	Rt = 4.36 min, [M+H] 500.
	Ethyl 6-{2-[2-[(4-chlorophenyl)methyl]oxy]-5-(trifluoromethyl)phenyl}-1-cyclopenten-1-yl]-3-methyl-2-pyridinecarboxylate	Rt = 4.49 min, [M+H] 516.
	Ethyl 6-{2-[2-[(2-fluorophenyl)methyl]oxy]-5-(trifluoromethyl)phenyl}-1-cyclopenten-1-yl]-3-methyl-2-pyridinecarboxylate	Rt = 4.39 min, [M+H] 500.

	Ethyl 6-{2-[2-{[(2,4-difluorophenyl)methyl]oxy}-5-(trifluoromethyl)phenyl]-1-cyclopenten-1-yl}-3-methyl-2-pyridinecarboxylate	Rt = 4.43 min, [M+H] 518.
	Ethyl 6-{2-[2-{[(2-chloro-4-fluorophenyl)methyl]oxy}-5-(trifluoromethyl)phenyl]-1-cyclopenten-1-yl}-3-methyl-2-pyridinecarboxylate	Rt = 4.58 min, [M+H] 534.
	Ethyl 6-{2-[2-{[(2,6-difluorophenyl)methyl]oxy}-5-(trifluoromethyl)phenyl]-1-cyclopenten-1-yl}-3-methyl-2-pyridinecarboxylate	Rt = 4.34 min, [M+H] 518.
	Ethyl 6-{2-[2-{[(2,3-difluorophenyl)methyl]oxy}-5-(trifluoromethyl)phenyl]-1-cyclopenten-1-yl}-3-methyl-2-pyridinecarboxylate	Rt = 4.39 min, [M+H] 518.
	Ethyl 6-{2-[2-{[(2-chloro-6-fluorophenyl)methyl]oxy}-5-(trifluoromethyl)phenyl]-1-cyclopenten-1-yl}-3-methyl-2-pyridinecarboxylate	Rt = 4.44 min, [M+H] 534.
	Ethyl 3-methyl-6-{2-[5-(trifluoromethyl)-2-{[(2,4,5-trifluorophenyl)methyl]oxy}phenyl]-1-cyclopenten-1-yl}-2-pyridinecarboxylate	Rt = 4.30 min, [M+H] 536.
	Ethyl 3-methyl-6-{2-[5-(trifluoromethyl)-2-{[(2,4,6-trifluorophenyl)methyl]oxy}phenyl]-1-cyclopenten-1-yl}-2-pyridinecarboxylate	Rt = 4.30 min, [M+H] 536.
	Ethyl 5-[2-(5-chloro-2-{[(2,4,5-trifluorophenyl)methyl]oxy}phenyl)-1-cyclopenten-1-yl]-2-methyl-3-pyridinecarboxylate	Rt=4.24, [MH+] 502.4

	Ethyl 5-[2-[5-chloro-2-((4-trifluoromethyl)phenyl)methyl]oxy]phenyl]-1-cyclopenten-1-yl]-2-methyl-3-pyridinecarboxylate	Rt=4.35 [MH+] 516.5, 518.4
	Ethyl 5-[2-(5-chloro-2-[(4-chlorophenyl)methyl]oxy)phenyl]-1-cyclopenten-1-yl]-2-methyl-3-pyridinecarboxylate	Rt=4.35 [MH+] 482.4
	Ethyl 5-[2-(5-chloro-2-[(2,3,6-trifluorophenyl)methyl]oxy)phenyl]-1-cyclopenten-1-yl]-2-methyl-3-pyridinecarboxylate	Rt=4.13 [MH+] 502.4, 504.4
	Ethyl 5-[2-(5-chloro-2-[(2-chloro-4-fluorophenyl)methyl]oxy)phenyl]-1-cyclopenten-1-yl]-2-methyl-3-pyridinecarboxylate	Rt=4.38 [MH+] 500.4
	Ethyl 5-[2-(5-chloro-2-[(2,4,6-trifluorophenyl)methyl]oxy)phenyl]-1-cyclopenten-1-yl]-2-methyl-3-pyridinecarboxylate	Rt=4.16 [MH+] 502.4, 504.4
	Ethyl 5-[2-[5-chloro-2-((2-fluoro-4-(trifluoromethyl)phenyl)methyl]oxy)phenyl]-1-cyclopenten-1-yl]-2-methyl-3-pyridinecarboxylate	Rt=4.38 [MH+] 534.5, 536.5
	Ethyl 5-[2-(2-[(4-bromophenyl)methyl]oxy)-5-chlorophenyl]-1-cyclopenten-1-yl]-2-methyl-3-pyridinecarboxylate	Rt=4.40 [MH+] 528.4, 530.4
	Ethyl 5-[2-(5-chloro-2-[(2,6-difluorophenyl)methyl]oxy)phenyl]-1-cyclopenten-1-yl]-2-methyl-3-pyridinecarboxylate	Rt=4.13 [MH+] 484.4, 486.5

	Ethyl 5-[2-(5-chloro-2-[(2-fluorophenyl)methyl]oxy)phenyl]-1-cyclopenten-1-yl]-2-methyl-3-pyridinecarboxylate	Rt=4.18 [MH+] 466.5, 468.5
	Ethyl 6-(2-(5-chloro-2-[(phenylmethyl)oxy]phenyl)-1-cyclopenten-1-yl)-3-(methylthio)-2-pyridinecarboxylate	Rt=4.24, [MH+] 480.4, 482.4
	Ethyl 6-[2-(5-chloro-2-[(2-fluorophenyl)methyl]oxy)phenyl]-1-cyclopenten-1-yl]-3-(methylthio)-2-pyridinecarboxylate	Rt=4.27 [MH+] 498.4, 500.4
	Ethyl 6-[2-(5-chloro-2-[(4-fluorophenyl)methyl]oxy)phenyl]-1-cyclopenten-1-yl]-3-(methylthio)-2-pyridinecarboxylate	Rt=4.27 [MH+] 498.4, 500.4
	Ethyl 6-[2-(5-chloro-2-[(2,4-difluorophenyl)methyl]oxy)phenyl]-1-cyclopenten-1-yl]-3-(methylthio)-2-pyridinecarboxylate	Rt=4.31 [MH+] 516.4, 518.4
	Ethyl 6-[2-(5-chloro-2-[(2,4,6-trifluorophenyl)methyl]oxy)phenyl]-1-cyclopenten-1-yl]-3-(methylthio)-2-pyridinecarboxylate	Rt=4.27 [MH+] 534.4, 536.4
	Ethyl 3-chloro-6-(2-(5-chloro-2-[(phenylmethyl)oxy]phenyl)-1-cyclopenten-1-yl)-2-pyridinecarboxylate	Rt=4.50, [MH+] 468.4
	Ethyl 3-chloro-6-[2-(5-chloro-2-[(4-fluorophenyl)methyl]oxy)phenyl]-1-cyclopenten-1-yl]-2-pyridinecarboxylate	Rt=4.49 [MH+] 486.4

	Ethyl 3-chloro-6-[2-(5-chloro-2-[(2-fluorophenyl)methoxy]phenyl)-1-cyclopenten-1-yl]-2-pyridinecarboxylate	Rt=4.45 [MH+] 486.4
	Ethyl 3-chloro-6-[2-(5-chloro-2-[(2,4-difluorophenyl)methoxy]phenyl)-1-cyclopenten-1-yl]-2-pyridinecarboxylate	Rt=4.52 [MH+] 504.4
	Ethyl 3-chloro-6-[2-(5-chloro-2-[(2,6-difluorophenyl)methoxy]phenyl)-1-cyclopenten-1-yl]-2-pyridinecarboxylate	Rt=4.46 [MH+] 504.4
	Ethyl 3-chloro-6-[2-(5-chloro-2-[(2,3,6-trifluorophenyl)methoxy]phenyl)-1-cyclopenten-1-yl]-2-pyridinecarboxylate	Rt=4.46 [MH+] 522.4
	Ethyl 3-chloro-6-[2-(5-chloro-2-[(2,4,5-trifluorophenyl)methoxy]phenyl)-1-cyclopenten-1-yl]-2-pyridinecarboxylate	Rt=4.55 [MH+] 522.4
	Ethyl 3-chloro-6-[2-(5-chloro-2-[(4-chlorophenyl)methoxy]phenyl)-1-cyclopenten-1-yl]-2-pyridinecarboxylate	Rt=4.65 [MH+] 502.4
	Ethyl 3-chloro-6-[2-(5-chloro-2-[(2-chloro-4-fluorophenyl)methoxy]phenyl)-1-cyclopenten-1-yl]-2-pyridinecarboxylate	Rt=4.70 [MH+] 522.3
	Ethyl 3-chloro-6-[2-(5-chloro-2-[(4-(trifluoromethyl)phenyl)methoxy]phenyl)-1-cyclopenten-1-yl]-2-pyridinecarboxylate	Rt=4.66 [MH+] 536.4

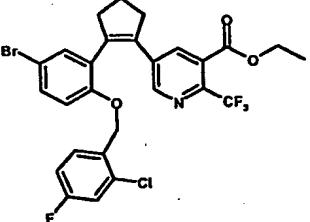
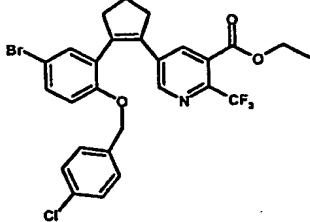
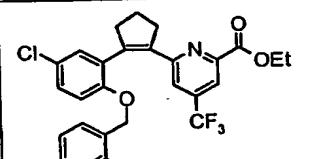
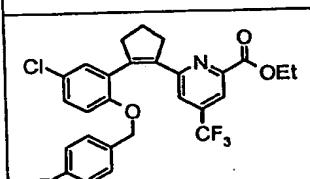
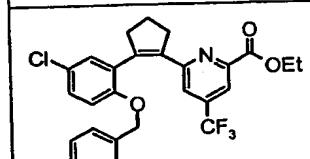
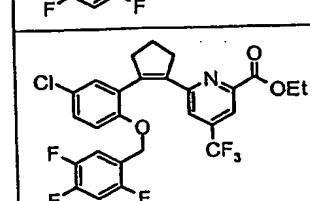
	Ethyl 3-chloro-6-{2-[5-chloro-2-({[2-fluoro-4-(trifluoromethyl)phenyl]methyl}oxy)phenyl]-1-cyclopenten-1-yl}-2-pyridinecarboxylate	Rt=4.69 [MH+] 554.4
	Ethyl 6-(2-{5-bromo-2-[(phenylmethyl)oxy]phenyl}-1-cyclopenten-1-yl)-3-chloro-2-pyridinecarboxylate	Rt=4.54, [MH+] 514.4
	Ethyl 6-[2-(5-bromo-2-[(4-fluorophenyl)methyl]oxy)phenyl]-1-cyclopenten-1-yl]-3-chloro-2-pyridinecarboxylate	Rt=4.10 [MH+] 532.3
	Ethyl 6-[2-(5-bromo-2-[(2,4-difluorophenyl)methyl]oxy)phenyl]-1-cyclopenten-1-yl]-3-chloro-2-pyridinecarboxylate	Rt=4.57 [MH+] 550.3
	Ethyl 6-[2-(5-bromo-2-[(2,3,6-trifluorophenyl)methyl]oxy)phenyl]-1-cyclopenten-1-yl]-3-chloro-2-pyridinecarboxylate	Rt=4.35 [MH+] 568.3
	Ethyl 6-[2-(5-bromo-2-[(4-chloro-2-fluorophenyl)methyl]oxy)phenyl]-1-cyclopenten-1-yl]-3-chloro-2-pyridinecarboxylate	Rt=4.60 [MH+] 566.3, 568.3
	Ethyl 6-[2-(5-bromo-2-[(2,3,4-trifluorophenyl)methyl]oxy)phenyl]-1-cyclopenten-1-yl]-3-chloro-2-pyridinecarboxylate	Rt=4.52 [MH+] 568.3
	Ethyl 6-(2-{5-chloro-2-[(phenylmethyl)oxy]phenyl}-1-cyclopenten-1-yl)-3-methyl-2-pyridinecarboxylate	Rt=4.40, [MH+] 448.5, 450.4
	Ethyl 6-[2-(5-chloro-2-[(2-fluorophenyl)methyl]oxy)phenyl]-1-cyclopenten-1-yl]-3-methyl-2-pyridinecarboxylate	Rt=4.42 [MH+] 466.5, 468.4

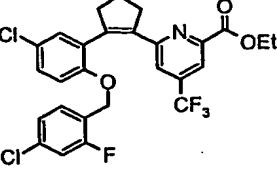
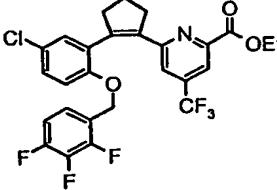
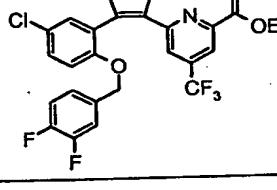
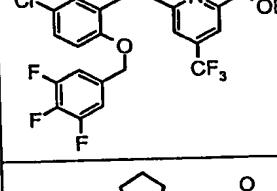
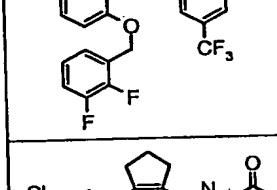
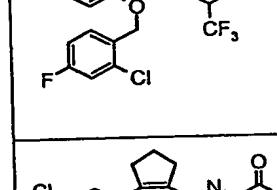
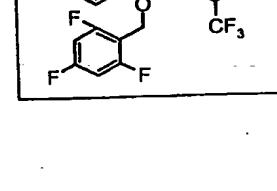
	Ethyl 6-[2-(5-chloro-2-{[(4-fluorophenyl)methyl]oxy}phenyl)-1-cyclopenten-1-yl]-3-methyl-2-pyridinecarboxylate	Rt=4.26 [MH+] 466.4, 468.4
	Ethyl 6-[2-(5-chloro-2-{[(2,4-difluorophenyl)methyl]oxy}phenyl)-1-cyclopenten-1-yl]-3-methyl-2-pyridinecarboxylate	Rt=4.09 [MH+] 484.4, 486.4
	Ethyl 6-[2-(5-chloro-2-{[(2,4,5-trifluorophenyl)methyl]oxy}phenyl)-1-cyclopenten-1-yl]-3-methyl-2-pyridinecarboxylate	Rt=4.49 [MH+] 502.4, 504.4
	Ethyl 6-[2-(5-chloro-2-{[(2,3-difluorophenyl)methyl]oxy}phenyl)-1-cyclopenten-1-yl]-3-methyl-2-pyridinecarboxylate	Rt=4.44 [MH+] 484.4, 486.4
	Ethyl 6-[2-(5-chloro-2-{[(3,4,5-trifluorophenyl)methyl]oxy}phenyl)-1-cyclopenten-1-yl]-3-methyl-2-pyridinecarboxylate	Rt=4.31 [MH+] 502.4, 504.4
	Ethyl 6-[2-(5-chloro-2-{[(2-chloro-6-fluorophenyl)methyl]oxy}phenyl)-1-cyclopenten-1-yl]-3-methyl-2-pyridinecarboxylate	Rt=4.18 [MH+] 500.4
	Ethyl 6-[2-(5-chloro-2-{[(2,4,6-trifluorophenyl)methyl]oxy}phenyl)-1-cyclopenten-1-yl]-3-methyl-2-pyridinecarboxylate	Rt=4.10 [MH+] 502.4, 504.4
	Ethyl 6-[2-(5-chloro-2-{[(2,6-difluorophenyl)methyl]oxy}phenyl)-1-cyclopenten-1-yl]-3-methyl-2-pyridinecarboxylate	Rt=4.15 [MH+] 484.4, 486.4
	Ethyl 6-[2-(5-chloro-2-{[(2-chloro-4-fluorophenyl)methyl]oxy}phenyl)-1-cyclopenten-1-yl]-3-methyl-2-pyridinecarboxylate	Rt=4.35 [MH+] 500.4

	Ethyl 6-[2-(5-chloro-2-[(4-chlorophenyl)methyl]oxy)phenyl]-1-cyclopenten-1-yl]-3-methyl-2-pyridinecarboxylate	Rt=4.33 [MH+] 482.4
	Ethyl 5-{2-[2-[(2-fluorophenyl)methyl]oxy]-5-(trifluoromethyl)phenyl}-1-cyclopenten-1-yl]-2-(trifluoromethyl)-3-pyridinecarboxylate	Rt = 4.49min [M+H] 554
	Ethyl 5-{2-[2-[(4-fluorophenyl)methyl]oxy]-5-(trifluoromethyl)phenyl}-1-cyclopenten-1-yl]-2-(trifluoromethyl)-3-pyridinecarboxylate	Rt = 4.49min [M+H] 554
	Ethyl 5-{2-[2-[(2,4-difluorophenyl)methyl]oxy]-5-(trifluoromethyl)phenyl}-1-cyclopenten-1-yl]-2-(trifluoromethyl)-3-pyridinecarboxylate	Rt = 3.88min [M+H] 572
	Ethyl 2-(trifluoromethyl)-5-[2-(5-(trifluoromethyl)-2-[(2,4,6-trifluorophenyl)methyl]oxy)phenyl]-1-cyclopenten-1-yl]-3-pyridinecarboxylate	Rt = 4.49min [M+H] 590
	Ethyl 5-{2-[2-[(2-chloro-4-fluorophenyl)methyl]oxy]-5-(trifluoromethyl)phenyl}-1-cyclopenten-1-yl]-2-(trifluoromethyl)-3-pyridinecarboxylate	Rt = 4.62min [M+H] 588(1Cl)
	Ethyl 6-{2-[2-[(phenylmethyl)oxy]-5-(trifluoromethyl)phenyl}-1-cyclopenten-1-yl]-4-(trifluoromethyl)-2-pyridinecarboxylate	Rt = 4.57min [M+H] 536

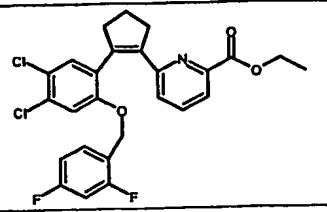
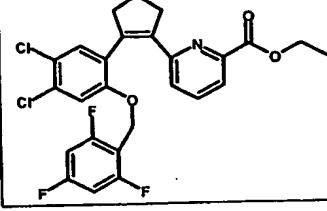
	Ethyl 6-{2-[2-[(2-fluorophenyl)methyl]oxy}-5-(trifluoromethyl)phenyl]-1-cyclopenten-1-yl}-4-(trifluoromethyl)-2-pyridinecarboxylate	Rt = 4.54min [M+H] 554
	Ethyl 6-{2-[2-[(4-fluorophenyl)methyl]oxy}-5-(trifluoromethyl)phenyl]-1-cyclopenten-1-yl}-4-(trifluoromethyl)-2-pyridinecarboxylate	Rt = 4.26min [M+H] 554
	Ethyl 6-{2-[2-[(2,4-difluorophenyl)methyl]oxy}-5-(trifluoromethyl)phenyl]-1-cyclopenten-1-yl}-4-(trifluoromethyl)-2-pyridinecarboxylate	Rt = 4.58min [M+H] 572
	Ethyl 4-(trifluoromethyl)-6-{2-[(5-(trifluoromethyl)-2-(trifluorophenyl)methyl]oxy}phenyl]-1-cyclopenten-1-yl}-2-pyridinecarboxylate	Rt = 4.56min [M+H] 590
	Ethyl 6-{2-[2-[(2-chloro-4-fluorophenyl)methyl]oxy}-5-(trifluoromethyl)phenyl]-1-cyclopenten-1-yl}-4-(trifluoromethyl)-2-pyridinecarboxylate	Rt = 4.71min [M+H] 588(1Cl)
	Ethyl 6-{2-[2-[(4-chloro-2-fluorophenyl)methyl]oxy}-5-(trifluoromethyl)phenyl]-1-cyclopenten-1-yl}-4-(trifluoromethyl)-2-pyridinecarboxylate	Rt = 4.18min [M+H] 588(1Cl)
	Ethyl 6-{2-[2-[(3,4-difluorophenyl)methyl]oxy}-5-(trifluoromethyl)phenyl]-1-cyclopenten-1-yl}-4-(trifluoromethyl)-2-pyridinecarboxylate	Rt = 4.58min [M+H] 572

	Ethyl 6-{2-[2-[(4-bromophenyl)methyl]oxy}-5-(trifluoromethyl)phenyl]-1-cyclopenten-1-yl}-4-(trifluoromethyl)-2-pyridinecarboxylate	Rt = 4.73min [M+H] 614, 616(1Br)
	Ethyl 4-(trifluoromethyl)-6-{2-[5-(trifluoromethyl)-2-((4-(trifluoromethyl)phenyl)methyl)oxy]phenyl}-1-cyclopenten-1-yl}-2-pyridinecarboxylate	Rt = 4.60min [M+H] 604
	Ethyl 6-{2-[2-[(2-chloro-4-fluorophenyl)methyl]oxy}-5-(trifluoromethyl)phenyl]-1-cyclopenten-1-yl}-4-(trifluoromethyl)-2-pyridinecarboxylate	[M+H] 599 Rt=4.34min
	Ethyl 5-[2-(5-bromo-2-((2-fluorophenyl)methyl)oxy)phenyl]-1-cyclopenten-1-yl]-2-(trifluoromethyl)-3-pyridinecarboxylate	[M+H] 565 Rt=4.21min
	Ethyl 5-[2-(5-bromo-2-((4-fluorophenyl)methyl)oxy)phenyl]-1-cyclopenten-1-yl]-2-(trifluoromethyl)-3-pyridinecarboxylate	[M+H] 565 Rt=4.21min
	Ethyl 5-[2-(5-bromo-2-((2,4-difluorophenyl)methyl)oxy)phenyl]-1-cyclopenten-1-yl]-2-(trifluoromethyl)-3-pyridinecarboxylate	[M+H] 583 Rt=4.37min
	Ethyl 5-[2-(5-bromo-2-((2,4,6-trifluorophenyl)methyl)oxy)phenyl]-1-cyclopenten-1-yl]-2-(trifluoromethyl)-3-pyridinecarboxylate	[M+H] 601 Rt=4.39min

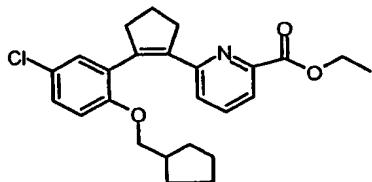
	ethyl 5-[2-(5-bromo-2-{[(2-chloro-4-fluorophenyl)methyl]oxy}phenyl)-1-cyclopenten-1-yl]-2-(trifluoromethyl)-3-pyridinecarboxylate	[M+H] 599 Rt=4.31min
	ethyl 5-[2-(5-bromo-2-{[(4-chlorophenyl)methyl]oxy}phenyl)-1-cyclopenten-1-yl]-2-(trifluoromethyl)-3-pyridinecarboxylate	[M+H] 581 Rt=4.39min
	Ethyl 6-(2-{5-chloro-2-[(phenylmethyl)oxy]phenyl}-1-cyclopenten-1-yl)-4-(trifluoromethyl)-2-pyridinecarboxylate	[M+H] 502.4, 504.4 Rt=4.58min
	Ethyl 6-[2-(5-chloro-2-{[(2-fluorophenyl)methyl]oxy}phenyl)-1-cyclopenten-1-yl]-4-(trifluoromethyl)-2-pyridinecarboxylate	[M+H] 520.4, 522.4 Rt=4.55min
	Ethyl 6-[2-(5-chloro-2-{[(4-fluorophenyl)methyl]oxy}phenyl)-1-cyclopenten-1-yl]-4-(trifluoromethyl)-2-pyridinecarboxylate	[M+H] 520.4, 522.4 Rt=4.57min
	Ethyl 6-[2-(5-chloro-2-{[(2,4-difluorophenyl)methyl]oxy}phenyl)-1-cyclopenten-1-yl]-4-(trifluoromethyl)-2-pyridinecarboxylate	[M+H] 538.4, 540.4 Rt=4.59min
	Ethyl 6-[2-(5-chloro-2-{[(2,4,5-trifluorophenyl)methyl]oxy}phenyl)-1-cyclopenten-1-yl]-4-(trifluoromethyl)-2-pyridinecarboxylate	[M+H] 556.3, 558.4 Rt=4.61min

	Ethyl 6-[2-(5-chloro-2-[(4-chloro-2-fluorophenyl)methoxy]phenyl)-1-cyclopenten-1-yl]-4-(trifluoromethyl)-2-pyridinecarboxylate	[M+H] 554.3, 556.4 Rt=4.73min
	Ethyl 6-[2-(5-chloro-2-[(2,3,4-trifluorophenyl)methoxy]phenyl)-1-cyclopenten-1-yl]-4-(trifluoromethyl)-2-pyridinecarboxylate	[M+H] 556.3, 558.4 Rt=4.61min
	Ethyl 6-[2-(5-chloro-2-[(3,4-difluorophenyl)methoxy]phenyl)-1-cyclopenten-1-yl]-4-(trifluoromethyl)-2-pyridinecarboxylate	[M+H] 538.4, 540.4 Rt=4.59min
	Ethyl 6-[2-(5-chloro-2-[(3,4,5-trifluorophenyl)methoxy]phenyl)-1-cyclopenten-1-yl]-4-(trifluoromethyl)-2-pyridinecarboxylate	[M+H] 556.3, 558.4 Rt=4.65min
	Ethyl 6-[2-(5-chloro-2-[(2,3-difluorophenyl)methoxy]phenyl)-1-cyclopenten-1-yl]-4-(trifluoromethyl)-2-pyridinecarboxylate	[M+H] 538.4, 540.4 Rt=4.57min
	Ethyl 6-[2-(5-chloro-2-[(2-chloro-4-fluorophenyl)methoxy]phenyl)-1-cyclopenten-1-yl]-4-(trifluoromethyl)-2-pyridinecarboxylate	[M+H] 554.3, 556.3 Rt=4.75min
	Ethyl 6-[2-(5-chloro-2-[(2,4,6-trifluorophenyl)methoxy]phenyl)-1-cyclopenten-1-yl]-4-(trifluoromethyl)-2-pyridinecarboxylate	[M+H] 556.3, 558.4 Rt=4.56min

	Ethyl 5-(2-{5-chloro-2-[(phenylmethyl)oxy]phenyl}-1-cyclopenten-1-yl)-3-pyridazinecarboxylate	[M+H] 435.2, 437.2, Rt=3.76min
	Ethyl 5-[2-(5-chloro-2-[(4-fluorophenyl)methyl]oxy)phenyl]-1-cyclopenten-1-yl]-3-pyridazinecarboxylate	[M+H] 453.3, 455.3, Rt=3.60min
	Ethyl 5-[2-(5-chloro-2-[(4-fluorophenyl)methyl]oxy)phenyl]-1-cyclopenten-1-yl]-3-pyridazinecarboxylate	[M+H] 471.3, 473.3, Rt=3.61min
	Ethyl 6-[2-(5-chloro-2-[(2,4-difluorophenyl)methyl]oxy)phenyl]-1-cyclopenten-1-yl]-3-pyridazinecarboxylate	Rt=4.27, [MH+] 470.3, 472.3
	Ethyl 2-[2-(5-chloro-2-[(2,4-difluorophenyl)methyl]oxy)phenyl]-1-cyclopenten-1-yl]-3-pyridazinecarboxylate	Rt=3.94, [MH+] 470.3, 472.3
	Ethyl 2-[2-(5-chloro-2-[(4-fluorophenyl)methyl]oxy)phenyl]-1-cyclopenten-1-yl]-3-pyridazinecarboxylate	Rt=3.90, [MH+] 452.3, 454.3
	Ethyl 6-[2-(5-chloro-2-[(2,4-difluorophenyl)methyl]oxy)phenyl]-1-cyclopenten-1-yl]-2-pyridinecarboxylate	Rt=4.20 [MH+] 470.3, 472.3
	Ethyl 6-(2-{4,5-dichloro-2-[(phenylmethyl)oxy]phenyl}-1-cyclopenten-1-yl)-2-pyridinecarboxylate	Rt=4.33 [MH+] 468.4, 470.4
	Ethyl 6-[2-(4,5-dichloro-2-[(2-fluorophenyl)methyl]oxy)phenyl]-1-cyclopenten-1-yl]-2-pyridinecarboxylate	Rt=4.35 [MH+] 486.4, 488.4

	Ethyl 6-[2-(4,5-dichloro-2-[(2,4-difluorophenyl)methoxy]phenyl)-1-cyclopenten-1-yl]-2-pyridinecarboxylate	Rt=4.36 [MH+] 504.4, 506.4
	Ethyl 6-[2-(4,5-dichloro-2-[(2,4,6-trifluorophenyl)methoxy]phenyl)-1-cyclopenten-1-yl]-2-pyridinecarboxylate	Rt=4.34 [MH+] 522.4, 524.4

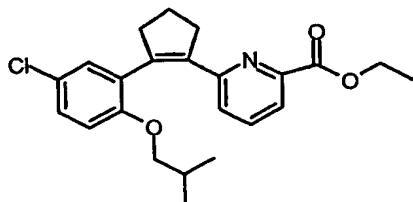
Ethyl 6-(2-{5-chloro-2-[cyclopentylmethyl]oxy}phenyl)-1-cyclopenten-1-yl)-2-pyridinecarboxylate



5 A mixture of 6-[2-(5-chloro-2-hydroxyphenyl)-1-cyclopenten-1-yl]-2-pyridinecarboxylic acid (100mg, 0.29mmol), potassium carbonate (200mg, 1.45mmol) and cyclopentylmethyl 4-methylbenzenesulfonate (90mg, 0.35mmol) in DMF (3ml) was heated at 90°C under nitrogen for 2 hours. More cyclopentylmethyl 4-methylbenzenesulfonate (40mg, 0.16mmol) was added and the mixture heated for another 2 hours. After cooling the solution was diluted with water and extracted with ethyl acetate (3x10ml). The combined extracts were dried (MgSO_4) and evaporated. Purification was carried out by flash chromatography (10% ethyl acetate:iso-hexane) to yield the title compound as a clear oil.

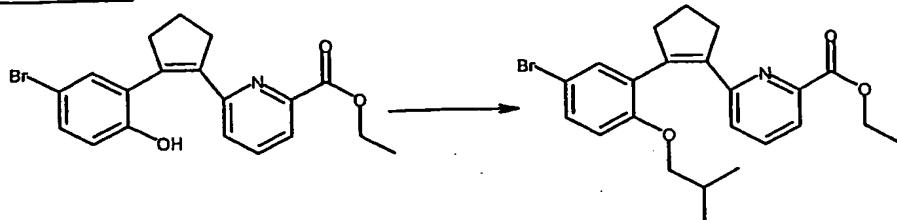
10 LC/MS: Rt = 4.68, [MH+] 426, 428

15 Ethyl 6-(2-{5-chloro-2-[(2-methylpropyl)oxy}phenyl)-1-cyclopenten-1-yl)-2-pyridinecarboxylate



Prepared in a similar manner to ethyl 6-(2-{5-chloro-2-[(cyclopentylmethyl)oxy}phenyl)-1-cyclopenten-1-yl)-2-pyridinecarboxylate using 1-bromo-2-methylpropane instead of cyclopentylmethyl 4-methylbenzenesulfonate. LC/MS: Rt=4.49 [MH+] 400, 402

Ethyl 6-(2-{5-bromo-2-[(1-methylethyl)oxy]phenyl}-1-cyclopenten-1-yl)-2-pyridinecarboxylate



A solution of ethyl 6-[2-(5-bromo-2-hydroxyphenyl)-1-cyclopenten-1-yl]-2-pyridinecarboxylate (125mg, 0.32mmol) in dry THF (2ml) was treated with diethyl azodicarboxylate (65mg, 67 μ l, 0.35mmol), triphenylphosphine (84mg, 0.35 mmol) and isobutyl alcohol (22mg, 27 μ l, 0.3mmol). The reaction mixture was stirred at room temperature overnight. The solvent was evaporated and the residue chromatographed using hexane/ethyl acetate 95:5 to give the title compound as a colourless oil.

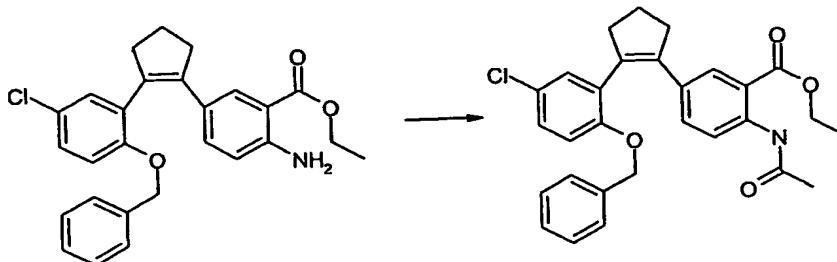
LCMS: Rt = 4.32 min. [M+H] = 444, 446.

The following intermediates were prepared by a similar route to Ethyl 6-(2-{5-bromo-2-[(1-methylethyl)oxy]phenyl}-1-cyclopenten-1-yl)-2-pyridinecarboxylate from the appropriate intermediates.

15

Structure	Name	LC/MS
	Ethyl 6-(2-{5-bromo-2-[(1-methylethyl)oxy]phenyl}-1-cyclopenten-1-yl)-2-pyridinecarboxylate	Rt = 3.96 min. [M+H] = 416, 418
	Ethyl 6-(2-{5-bromo-2-[(cyclopentylmethyl)oxy]phenyl}-1-cyclopenten-1-yl)-2-pyridinecarboxylate	Rt = 4.52 min. [M+H] = 470, 472
	Ethyl 6-(2-{5-bromo-2-[(cyclohexylmethyl)oxy]phenyl}-1-cyclopenten-1-yl)-2-pyridinecarboxylate	Rt = 4.64min [M+H] = 484, 486

Ethyl 2-(acetylamino)-5-(2-{5-chloro-2-[(phenylmethyl)oxy]phenyl}-1-cyclopenten-1-yl)benzoate



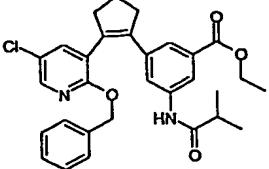
A mixture of ethyl 2-amino-5-(2-{5-chloro-2-[(phenylmethyl)oxy]phenyl}-1-cyclopenten-1-yl)benzoate (75mg, 0.17mmol), acetyl chloride (21mg, 0.3mmol), and triethylamine (30g, 42µl, 0.3mmol) in dichloromethane (3 ml) was stirred at room temperature for 30 mins.

5 The solvent was evaporated and the residue was chromatographed eluting with ethyl acetate/hexane 1:4 to give the title compound as a colourless glass.

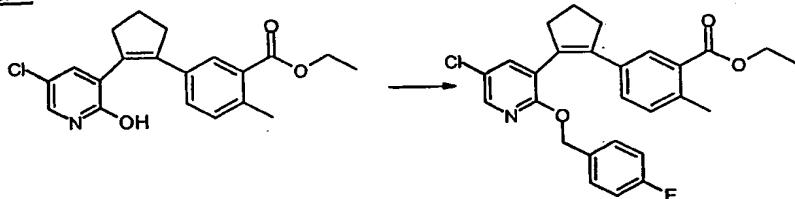
Rt = 4.08 min. [M+H] = 490

10 The following intermediates were prepared by a similar route to ethyl 2-(acetylamino)-5-(2-{5-chloro-2-[(phenylmethyl)oxy]phenyl}-1-cyclopenten-1-yl)benzoate from the appropriate intermediates.

Structure	Name	LC/MS
	Ethyl 2-(acetylamino)-5-[2-(5-chloro-2-[(4-fluorophenyl)methyl]oxy)phenyl]-1-cyclopenten-1-yl]benzoate	Rt = 4.09 min. [M+H] = 508
	Ethyl 2-(acetylamino)-5-[2-(5-chloro-2-[(2,4-difluorophenyl)methyl]oxy)phenyl]-1-cyclopenten-1-yl]benzoate	Rt = 4.11 min. [M+H] = 526
	Ethyl 3-(acetylamino)-5-(2-{5-chloro-2-[(phenylmethyl)oxy]3-pyridinyl}-1-cyclopenten-1-yl)benzoate	Rt = 4.04 min [M+H] = 491
	Ethyl 3-(2-{5-chloro-2-[(phenylmethyl)oxy]3-pyridinyl}-1-cyclopenten-1-yl)-5-(propanoylamino)benzoate	Rt = 4.03 min. [M+H] = 505

	Ethyl 3-(2-{5-chloro-2-[(phenylmethyl)oxy]-3-pyridinyl}-1-cyclopenten-1-yl)-5-[(2-methylpropanoyl)amino]benzoate	Rt = 4.25 min. [M+H] = 519
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Ethyl 5-[2-(5-chloro-2-[(4-fluorophenyl)methyl]oxy)-3-pyridinyl]-1-cyclopenten-1-yl]-2-methylbenzoate

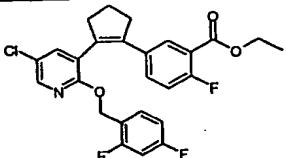
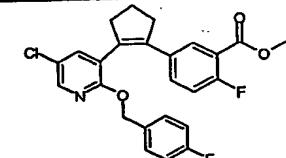
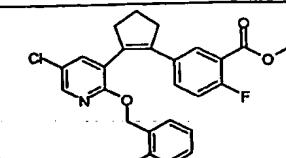


5 Ethyl 5-[2-(5-chloro-2-oxo-1,2-dihydro-3-pyridinyl)-1-cyclopenten-1-yl]-2-methylbenzoate (76mg, 0.213mmol) was dissolved in toluene (3ml) and silver carbonate (65mg, 0.234mmol) and 4-fluorobenzyl bromide (29μl, 0.234mmol) added. The mixture was heated to reflux for 1 hour then stirred at room temperature for 16 hours. After filtration, the solution was washed with water, dried (MgSO_4) and evaporated. The residue was flash chromatographed eluting with 2% ethyl acetate/iso hexane to give the title compound (47mg). LC/MS Rt=4.47min $[\text{MH}^+] 466, 468.$

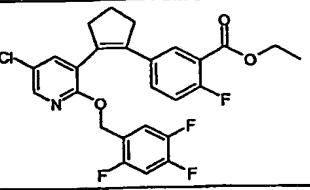
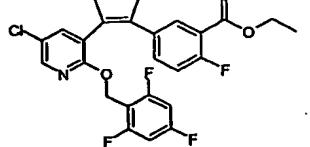
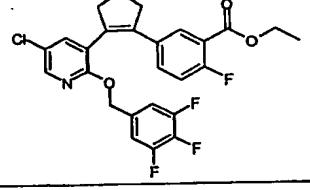
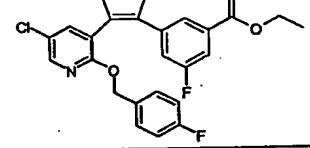
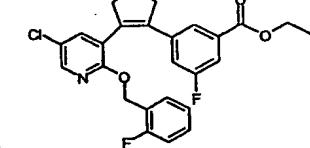
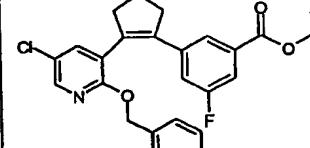
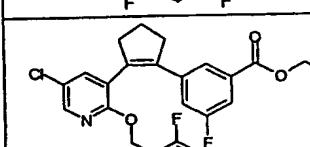
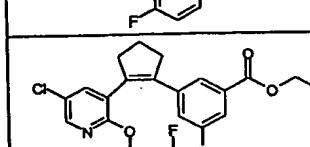
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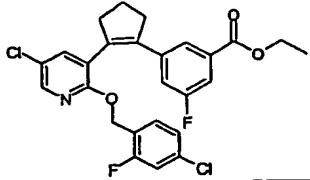
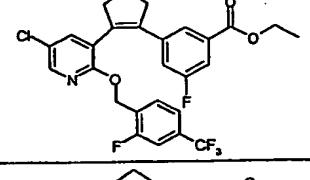
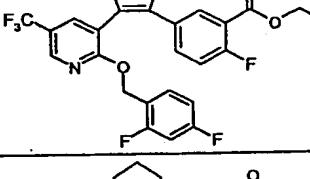
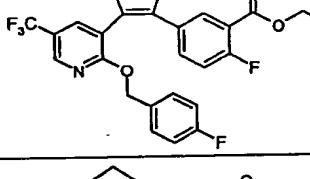
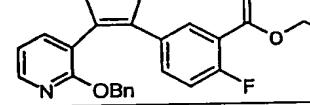
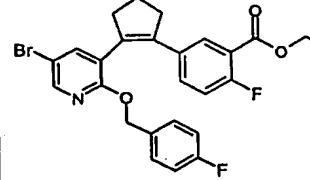
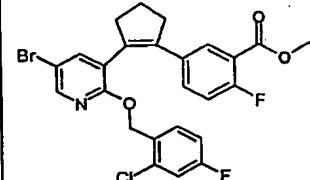
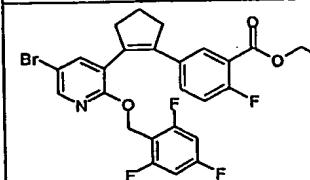
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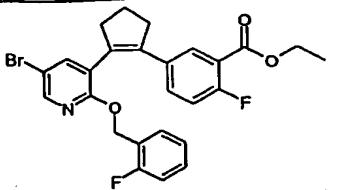
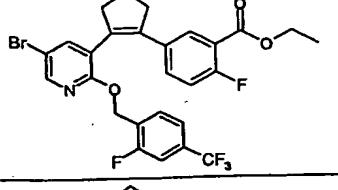
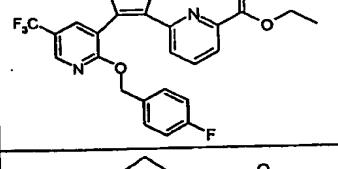
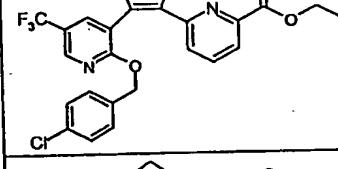
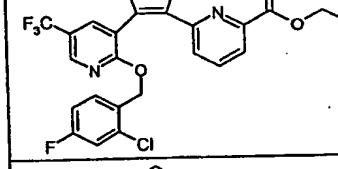
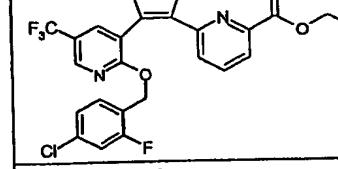
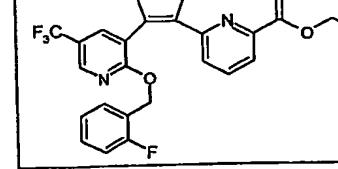
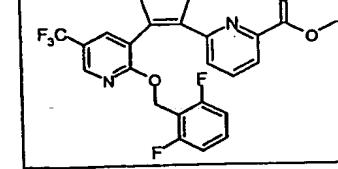
The following intermediates were prepared by a similar route to ethyl 5-[2-(5-chloro-2-[(4-fluorophenyl)methyl]oxy)-3-pyridinyl]-1-cyclopenten-1-yl]-2-methylbenzoate from the appropriate intermediates.

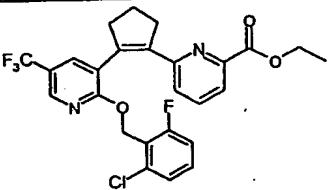
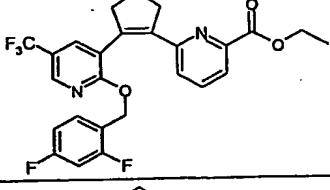
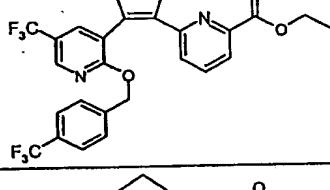
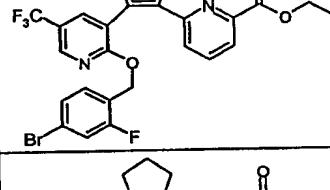
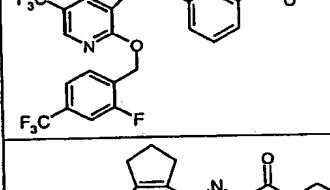
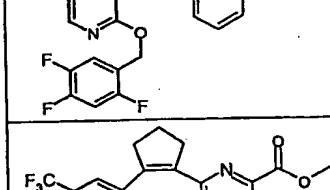
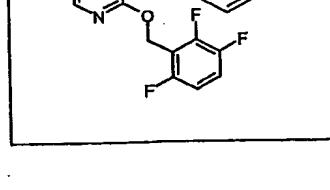
	COMPOUND NAME	LC/MS
	Ethyl 5-[2-(5-chloro-2-[(2,4-difluorophenyl)methyl]oxy)-3-pyridinyl]-1-cyclopenten-1-yl]-2-fluorobenzoate	Rt = 4.46min. $[\text{MH}^+] 488, 490.$
	Ethyl 5-[2-(5-chloro-2-[(4-fluorophenyl)methyl]oxy)-3-pyridinyl]-1-cyclopenten-1-yl]-2-fluorobenzoate	Rt = 4.42min. $[\text{MH}^+] 470, 472.$
	Ethyl 5-[2-(5-chloro-2-[(2-fluorophenyl)methyl]oxy)-3-pyridinyl]-1-cyclopenten-1-yl]-2-fluorobenzoate	Rt = 4.50min. $[\text{MH}^+] 470, 472.$

	Ethyl 5-[2-(5-chloro-2-[(2,3-difluorophenyl)methyl]oxy)-3-pyridinyl]-1-cyclopenten-1-yl]-2-fluorobenzoate	Rt = 4.40min. [MH ⁺] 488, 490.
	Ethyl 5-[2-(5-chloro-2-[(3,4-difluorophenyl)methyl]oxy)-3-pyridinyl]-1-cyclopenten-1-yl]-2-fluorobenzoate	Rt = 4.44min. [MH ⁺] 488, 490.
	Ethyl 5-[2-(5-chloro-2-[(2,5-difluorophenyl)methyl]oxy)-3-pyridinyl]-1-cyclopenten-1-yl]-2-fluorobenzoate	Rt = 4.43min. [MH ⁺] 488, 490.
	Ethyl 5-[2-[5-chloro-2-((2-fluoro-4-(trifluoromethyl)phenyl)methyl]oxy)-3-pyridinyl]-1-cyclopenten-1-yl]-2-fluorobenzoate	Rt = 4.32min. [MH ⁺] 538, 540.
	Ethyl 5-[2-(5-chloro-2-[(4-chloro-2-fluorophenyl)methyl]oxy)-3-pyridinyl]-1-cyclopenten-1-yl]-2-fluorobenzoate	Rt = 4.32min. [MH ⁺] 504, 506.
	Ethyl 5-[2-(5-chloro-2-[(2-chloro-4-fluorophenyl)methyl]oxy)-3-pyridinyl]-1-cyclopenten-1-yl]-2-fluorobenzoate	Rt = 4.50min. [MH ⁺] 504, 506.
	Ethyl 5-[2-(5-chloro-2-[(2,3,4-trifluorophenyl)methyl]oxy)-3-pyridinyl]-1-cyclopenten-1-yl]-2-fluorobenzoate	Rt = 4.43min. [MH ⁺] 506, 508.
	Ethyl 5-[2-(5-chloro-2-[(2,3,6-trifluorophenyl)methyl]oxy)-3-pyridinyl]-1-cyclopenten-1-yl]-2-fluorobenzoate	Rt = 4.55min. [MH ⁺] 506, 508.

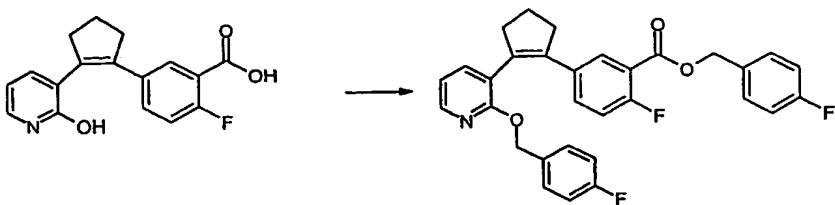
	Ethyl 5-[2-(5-chloro-2-[(2,4,5-trifluorophenyl) methyl]oxy)-3-pyridinyl]-1-cyclopenten-1-yl]-2-fluorobenzoate	Rt = 4.62min. [MH ⁺] 506, 508.
	Ethyl 5-[2-(5-chloro-2-[(2,4,6-trifluorophenyl) methyl]oxy)-3-pyridinyl]-1-cyclopenten-1-yl]-2-fluorobenzoate	Rt = 4.40min. [MH ⁺] 506, 508.
	Ethyl 5-[2-(5-chloro-2-[(3,4,5-trifluorophenyl) methyl]oxy)-3-pyridinyl]-1-cyclopenten-1-yl]-2-fluorobenzoate	Rt = 4.49min. [MH ⁺] 506, 508.
	Ethyl 3-[2-(5-chloro-2-[(4-fluorophenyl) methyl]oxy)-3-pyridinyl]-1-cyclopenten-1-yl]-5-fluorobenzoate	Rt = 4.36min. [MH ⁺] 470, 472.
	Ethyl 3-[2-(5-chloro-2-[(2-fluorophenyl) methyl]oxy)-3-pyridinyl]-1-cyclopenten-1-yl]-5-fluorobenzoate	Rt = 4.38min. [MH ⁺] 470, 472.
	Ethyl 3-[2-(5-chloro-2-[(2,4-difluorophenyl) methyl]oxy)-3-pyridinyl]-1-cyclopenten-1-yl]-5-fluorobenzoate	Rt = 4.50min. [MH ⁺] 488, 490.
	Ethyl 3-[2-(5-chloro-2-[(2,6-difluorophenyl) methyl]oxy)-3-pyridinyl]-1-cyclopenten-1-yl]-5-fluorobenzoate	Rt = 4.50min. [MH ⁺] 488, 490.
	Ethyl 3-[2-(5-chloro-2-[(2,4,6-trifluorophenyl) methyl]oxy)-3-pyridinyl]-1-cyclopenten-1-yl]-5-fluorobenzoate	Rt = 4.53min. [MH ⁺] 506, 508.

	Ethyl 3-[2-(5-chloro-2-{[(4-chloro-2-fluoro phenyl)methyl]oxy}-3-pyridinyl)-1-cyclopenten-1-yl]-5-fluorobenzoate	Rt = 4.72min. [MH ⁺] 504, 506.
	Ethyl 3-[2-[5-chloro-2-({[2-fluoro-4-(trifluoromethyl)phenyl]methyl}oxy)-3-pyridinyl]-1-cyclopenten-1-yl]-5-fluorobenzoate	Rt = 4.72min. [MH ⁺] 538, 540.
	Ethyl 5-[2-[2-{{(2,4-difluorophenyl)methyl}oxy}-5-(trifluoromethyl)-3-pyridinyl]-1-cyclopenten-1-yl]-2-fluorobenzoate	Rt = 4.44min. [MH ⁺] 522.
	Ethyl 2-fluoro-5-{2-[2-{{(4-fluorophenyl)methyl}oxy}-5-(trifluoromethyl)-3-pyridinyl]-1-cyclopenten-1-yl}benzoate	Rt = 4.41min. [MH ⁺] 504.
	Ethyl 2-fluoro-5-(2-{{(phenylmethyl)oxy}-3-pyridinyl}-1-cyclopenten-1-yl)benzoate	Rt = 4.14min. [MH ⁺] 418.
	Ethyl 5-[2-(5-bromo-2-{[(4-fluorophenyl) methyl}oxy)-3-pyridinyl]-1-cyclopenten-1-yl]-2-fluorobenzoate	Rt = 4.36min. [MH ⁺] 514, 516.
	Ethyl 5-[2-(5-bromo-2-{[(2-chloro-4-fluoro phenyl)methyl}oxy)-3-pyridinyl]-1-cyclopenten-1-yl]-2-fluorobenzoate	Rt = 4.64min. [MH ⁺] 548, 550.
	Ethyl 5-[2-(5-bromo-2-{[(2,4,6-trifluorophenyl) methyl}oxy)-3-pyridinyl]-1-cyclopenten-1-yl]-2-fluorobenzoate	Rt = 4.44min. [MH ⁺] 550, 552.

	Ethyl 5-[2-(5-bromo-2-[(2-fluorophenyl)methoxy]-3-pyridinyl)-1-cyclopenten-1-yl]-2-fluorobenzoate	Rt = 3.86min. [MH ⁺] 514, 516.
	Ethyl 5-[2-(5-bromo-2-[(2-fluoro-4-(trifluoromethyl)phenyl)methoxy]-3-pyridinyl)-1-cyclopenten-1-yl]-2-fluorobenzoate	Rt = 4.61min. [MH ⁺] 582, 584.
	Ethyl 6-(2-{2-[4-fluoro(phenyl)methoxy]-5-(trifluoromethyl)pyridin-3-yl}-1-cyclopenten-1-yl)-2-pyridinecarboxylate	LC/MS Rt=4.11min [MH ⁺] 487.
	Ethyl 6-[2-{2-[(4-chlorophenyl)methoxy]-5-(trifluoromethyl)-3-pyridinyl}-1-cyclopenten-1-yl]-2-pyridinecarboxylate	Rt=4.24min [MH ⁺] 503
	Ethyl 6-[2-{2-[(2-chloro-4-fluorophenyl)methoxy]-5-(trifluoromethyl)-3-pyridinyl}-1-cyclopenten-1-yl]-2-pyridinecarboxylate	Rt=4.28min [MH ⁺] 521
	Ethyl 6-[2-{2-[(4-chloro-2-fluorophenyl)methoxy]-5-(trifluoromethyl)-3-pyridinyl}-1-cyclopenten-1-yl]-2-pyridinecarboxylate	Rt=4.28min [MH ⁺] 521
	Ethyl 6-[2-{2-[(2-fluorophenyl)methoxy]-5-(trifluoromethyl)-3-pyridinyl}-1-cyclopenten-1-yl]-2-pyridinecarboxylate	Rt=4.11min [MH ⁺] 487
	Ethyl 6-[2-{2-[(2,6-difluorophenyl)methoxy]-5-(trifluoromethyl)-3-pyridinyl}-1-cyclopenten-1-yl]-2-pyridinecarboxylate	Rt=4.08min [MH ⁺] 505

	Ethyl 6-{2-[2-[(2-chloro-6-fluorophenyl)methyl]oxy}-5-(trifluoromethyl)-3-pyridinyl]-1-cyclopenten-1-yl]-2-pyridinecarboxylate	Rt=4.20min [MH ⁺] 521
	Ethyl 6-{2-[2-[(2,4-difluorophenyl)methyl]oxy}-5-(trifluoromethyl)-3-pyridinyl]-1-cyclopenten-1-yl]-2-pyridinecarboxylate	Rt=4.13min [MH ⁺] 505
	Ethyl 6-{2-[5-(trifluoromethyl)-2-((4-(trifluoromethyl)phenyl)methyl)oxy}-3-pyridinyl]-1-cyclopenten-1-yl]-2-pyridinecarboxylate	Rt=4.25min [MH ⁺] 537
	Ethyl 6-{2-[2-[(4-bromo-2-fluorophenyl)methyl]oxy}-5-(trifluoromethyl)-3-pyridinyl]-1-cyclopenten-1-yl]-2-pyridinecarboxylate	Rt=4.31min [MH ⁺] 565, 567
	Ethyl 6-{2-[2-((2-fluoro-4-(trifluoromethyl)phenyl)methyl)oxy}-5-(trifluoromethyl)-3-pyridinyl]-1-cyclopenten-1-yl]-2-pyridinecarboxylate	Rt=4.29min [MH ⁺] 555
	Ethyl 6-{2-((5-(trifluoromethyl)-2-((2,4,5-trifluorophenyl)methyl)oxy)-3-pyridinyl)-1-cyclopenten-1-yl]-2-pyridinecarboxylate	Rt=4.17min [MH ⁺] 523
	Ethyl 6-{2-((5-(trifluoromethyl)-2-((2,3,6-trifluorophenyl)methyl)oxy)-3-pyridinyl)-1-cyclopenten-1-yl]-2-pyridinecarboxylate	Rt=4.10min [MH ⁺] 523

(4-Fluorophenyl)methyl 2-fluoro-5-[2-(2-[(4-fluorophenyl)methyl]oxy)-3-pyridinyl]-1-cyclopenten-1-yl]benzoate

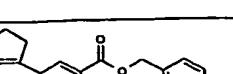


2-Fluoro-5-[2-(2-oxo-1,2-dihydro-3-pyridinyl)-1-cyclopenten-1-yl]benzoic acid (65mg, 0.217mmol) was dissolved in toluene (2ml) and silver carbonate (132mg, 0.478mmol) and 4-fluorobenzyl bromide (60μl, 0.478mmol) added. The mixture was heated to reflux for 16 hours. After filtration and dilution with ethyl acetate, the solution was washed with water, dried (MgSO_4) and evaporated. The residue was flash chromatographed eluting with 3% ethyl acetate/isohexane to give the title compound (32mg).

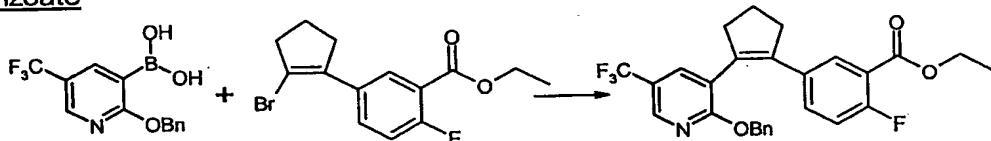
LC/MS Rt=4.40min [MH⁺] 516.

10 The following intermediates were prepared by a similar route to (4-fluorophenyl)methyl 2-fluoro-5-[2-(2-{[(4-fluorophenyl)methyl]oxy}-3-pyridinyl)-1-cyclopenten-1-yl]benzoate from the appropriate intermediates.

Structure	COMPOUND NAME	LCMS
	(2,4-Difluorophenyl) methyl 5-[2-(2-{[(2,4-difluorophenyl)methyl]oxy}-3-pyridinyl)-1-cyclopenten-1-yl]-2-fluorobenzoate	Rt=4.64min [MH ⁺] 552.
	(4-Fluorophenyl)methyl 2-fluoro-5-[2-(2-{[(4-fluorophenyl)methyl]oxy}-3-pyridinyl)-1-cyclopenten-1-yl]benzoate	Rt=4.37min [MH ⁺] 516.
	Phenylmethyl 5-(2-{5-bromo-2-[(phenylmethyl)oxy]-3-pyridinyl}-1-cyclopenten-1-yl)-2-fluorobenzoate	Rt=4.64min [MH ⁺] 558, 560.
	(2,4-Difluorophenyl) methyl 5-[2-(5-bromo-2-{[(2,4-difluorophenyl)methyl]oxy}-3-pyridinyl)-1-cyclopenten-1-yl]-2-fluorobenzoate	Rt=4.66min [MH ⁺] 630, 632.
	Phenylmethyl 6-(2-{[(phenylmethyl)oxy]-3-pyridinyl}-1-cyclopenten-1-yl)-2-pyridinecarboxylate	Rt=4.04min [MH ⁺] 463.

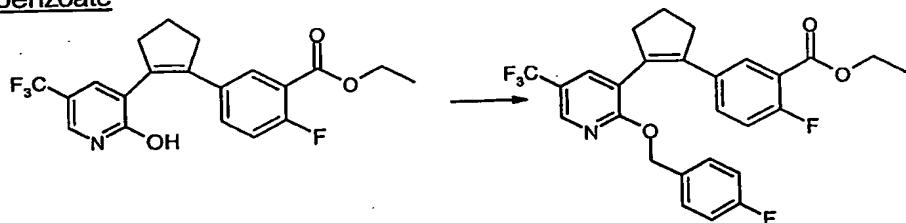
	(4-Fluorophenyl)methyl 3-[2-(5-bromo-2-[(4-fluorophenyl)methyl]oxy)-3-pyridinyl]-1-cyclopenten-1-yl benzoate	Rt = 4.63min [MH ⁺] 576, 578
	(2,4-Difluorophenyl)methyl 3-[2-(5-bromo-2-[(2,4-difluorophenyl)methyl]oxy)-3-pyridinyl]-1-cyclopenten-1-yl benzoate	Rt = 4.46min [MH ⁺] 612, 614

Ethyl 2-fluoro-5-{2-[2-(phenylmethoxy)-5-(trifluoromethyl)pyridin-3-yl]cyclopent-1-en-1-yl}benzoate



5 2-(Phenylmethoxy)-5-(trifluoromethyl)pyridine-3-boronic acid (10.32g, 34.7mmol) and ethyl
 10 5-(2-bromocyclopent-1-enyl)-2-fluorobenzoate (5.44g, 17.4mmol) were dissolved in
 dimethoxyethane (120mL) under nitrogen, and Pd(PPh_3)₄ (1.00g, 0.87mmol) and 2N
 aqueous sodium carbonate solution (60ml) were added. The mixture was heated at 80°C
 for 18hours, but TLC analysis showed incomplete reaction. Further Pd(PPh_3)₄ was added
 and heating was continued for 3 hours. After cooling, the solvents were removed *in vacuo*,
 and the residue was partitioned between diethyl ether and water. The aqueous was
 extracted with further ether, and the combined organic extracts were dried (Na_2SO_4) and
 concentrated *in vacuo*. The resulting dark brown oil was purified by flash chromatography
 on silica (gradient elution, 0-6% ethyl acetate/cyclohexane) to give the title compound
 15 (7.02g). LC/MS Rt=4.23min [MH^+] 485.

Ethyl 2-fluoro-5-(2-[2-[(4-fluorophenyl)methoxy]-5-(trifluoromethyl)pyridin-3-yl]cyclopent-1-en-1-yl)-benzoate



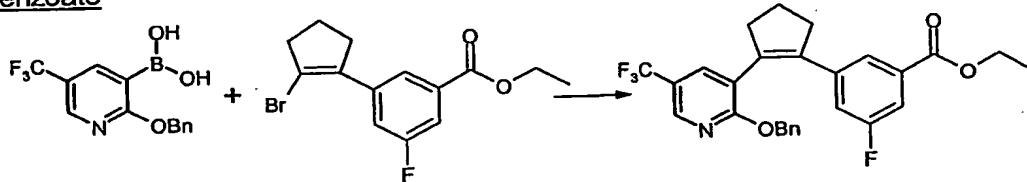
20 Ethyl 2-fluoro-5-{2-[2-hydroxy-5-(trifluoromethyl)pyridin-3-yl]cyclopent-1-en-1-yl}benzoate (250mg, 0.633mmol) was dissolved in toluene (4ml), and silver carbonate (210mg, 0.764mmol) and 4-fluorobenzyl bromide (130mg, 1.45mmol) added. The mixture was heated to reflux for 5.5 hours. The mixture was concentrated *in vacuo*, and the residue was partitioned between water and dichloromethane. The organic extract was

concentrated *in vacuo*. The residue was purified by flash chromatography on silica (gradient elution, 0-4% ethyl acetate/cyclohexane) to give the title compound.. LC/MS Rt=4.31min [MH⁺] 504.

5 The following compounds (table) were prepared by the same method from ethyl 2-fluoro-5-{2-[2-hydroxy-5-(trifluoromethyl)pyridin-3-yl]cyclopent-1-en-1-yl}benzoate by reaction with appropriately substituted benzyl bromides.

STRUCTURE	COMPOUND NAME	LCMS
	Ethyl 5-(2-{2-[2,4-difluorophenyl]methoxy}-5-(trifluoromethyl)pyridin-3-yl)cyclopent-1-en-1-yl)-2-fluorobenzoate	Rt= 4.33min [MH ⁺] 522
	Ethyl 2-fluoro-5-(2-{2-[2-fluorophenyl]methoxy}-5-(trifluoromethyl)pyridin-3-yl)cyclopent-1-en-1-yl)-benzoate	Rt= 4.32min [MH ⁺] 504
	Ethyl 5-(2-{2-[2,6-difluorophenyl]methoxy}-5-(trifluoromethyl)pyridin-3-yl)cyclopent-1-en-1-yl)-2-fluorobenzoate	Rt= 4.30min [MH ⁺] 522
	Ethyl 5-(2-{2-[2-chloro-4-fluorophenyl]methoxy}-5-(trifluoromethyl)pyridin-3-yl)cyclopent-1-en-1-yl)-2-fluorobenzoate	Rt= 4.45min [MH ⁺] 539

10 Ethyl 3-fluoro-5-{2-[2-(phenylmethoxy)-5-(trifluoromethyl)pyridin-3-yl]cyclopent-1-en-1-yl}benzoate

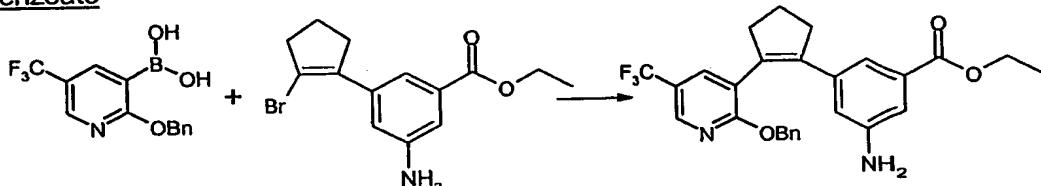


15 2-(Phenylmethoxy)-5-(trifluoromethyl)pyridine-3-boronic acid (10.53g, 33.6mmol) and ethyl 2-(bromocyclopent-1-enyl)-3-fluorobenzoate (5.93g, 20.0mmol) were dissolved in dimethoxyethane (120mL) under nitrogen, and Pd(PPh₃)₄ (1.15g, 1.0mmol) and 2N aqueous sodium carbonate solution (60ml) were added. The mixture was heated at 80°C

for 18hours. After cooling, the solvents were removed *in vacuo*, and the residue was partitioned between diethyl ether and water. The aqueous was extracted with further ether, and the combined organic layers were dried (Na_2SO_4) and concentrated *in vacuo*. The resulting dark brown oil was purified by flash chromatography on silica (gradient elution, 0-4% ethyl acetate/cyclohexane) to give the title compound (7.42g).

5 LC/MS Rt=4.32min [MH^+] 485.

Ethyl 3-amino-5-{2-[2-(phenylmethoxy)-5-(trifluoromethyl)pyridin-3-yl]cyclopent-1-en-1-yl}benzoate

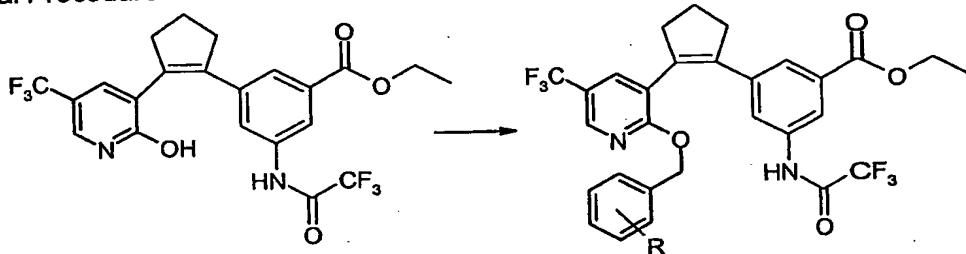


10 2-(Phenylmethoxy)-5-(trifluoromethyl)pyridine-3-boronic acid (6.0g, 20.2mmol) and ethyl 3-amino-5-(2-bromocyclopent-1-enyl)benzoate (3.16g, 10.1mmol) were dissolved in dimethoxyethane (50mL) under nitrogen, and $\text{Pd}(\text{PPh}_3)_4$ (0.58g, 0.5mmol) and 2N aqueous sodium carbonate solution (10ml) were added. The mixture was heated at 80°C for 18hours. After cooling, the solvents were removed *in vacuo*, and the residue was partitioned between diethyl ether and water. The aqueous was extracted with further ether (x2), and the combined organic layers were dried (Na_2SO_4) and concentrated *in vacuo*.

15 The resulting dark brown oil was purified using an acidic solid phase cartridge (Isolute® Flash SCX-2, 50g), loading the crude material as a methanol solution and eluting with 10% aqueous ammonia in methanol. Concentration of the relevant fractions *in vacuo* gave the title compound (4.01g). LC/MS Rt=4.01min [MH^+] 483.

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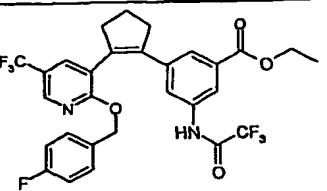
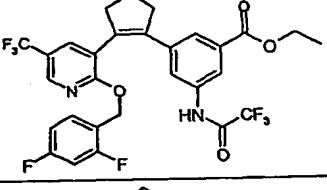
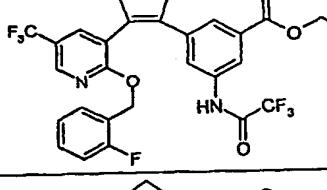
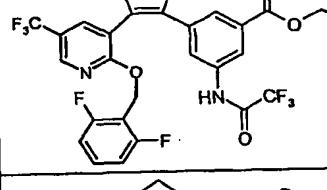
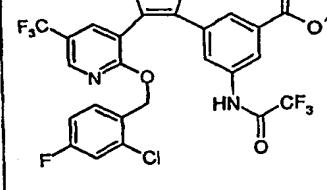
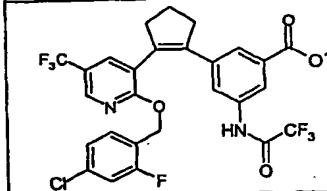
General Procedure

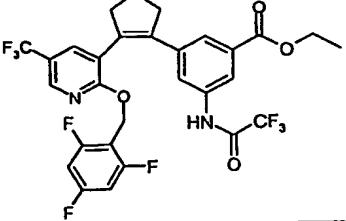
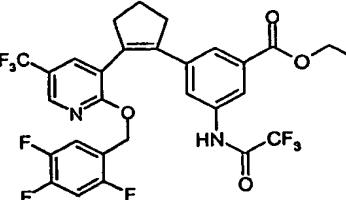
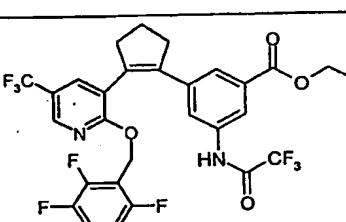
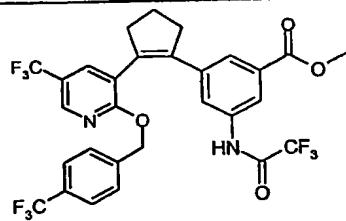
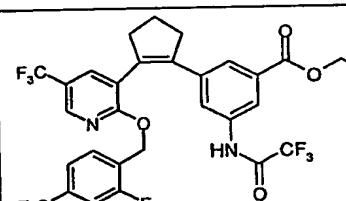
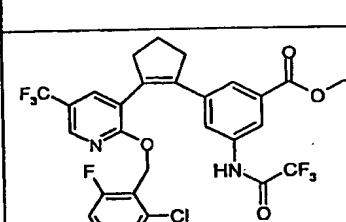


25 Ethyl 5-{2-[2-(hydroxy)-5-(trifluoromethyl)pyridin-3-yl]cyclopent-1-en-1-yl}-3-(trifluoroacetamido)benzoate (122mg, 0.25mmol) was dissolved in toluene (4ml), together with silver carbonate (76mg, 0.275mmol) and a substituted benzyl bromide (1.1equiv.), and this was heated to reflux for 18 hours. The mixture was filtered and concentrated *in vacuo*. The residue was purified by flash chromatography on silica (gradient elution, 0-10% ethyl acetate/cyclohexane).

30

The following compounds were prepared by the above General Procedure from ethyl 2-fluoro-5-{2-[2-hydroxy-5-(trifluoromethyl)pyridin-3-yl]cyclopent-1-en-1-yl}benzoate by reaction with appropriately substituted benzyl bromides.

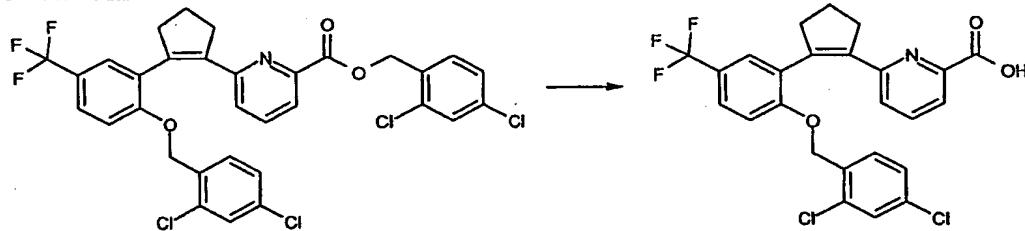
	COMPOUND NAME	LCMS
	Ethyl 5-(2-{2-[4-(trifluoromethyl)phenyl]methoxy}-5-(trifluoromethyl)pyridin-3-yl)cyclopent-1-en-1-yl)-3-(trifluoroacetamido)benzoate	Rt= 4.27min [MH ⁺] 597
	Ethyl 5-(2-{2-[2,4-difluorophenyl]methoxy}-5-(trifluoromethyl)pyridin-3-yl)cyclopent-1-en-1-yl)-3-(trifluoroacetamido)benzoate	Rt= 4.29min [MH ⁺] 615
	Ethyl 5-(2-{2-[2-fluorophenyl]methoxy}-5-(trifluoromethyl)pyridin-3-yl)cyclopent-1-en-1-yl)-3-(trifluoroacetamido)benzoate	Rt= 4.28min [MH ⁺] 597
	Ethyl 5-(2-{2-[2,6-difluorophenyl]methoxy}-5-(trifluoromethyl)pyridin-3-yl)cyclopent-1-en-1-yl)-3-(trifluoroacetamido)benzoate	Rt= 4.25min [MH ⁺] 615
	Ethyl 5-(2-{2-[2-chloro-4-fluorophenyl]methoxy}-5-(trifluoromethyl)pyridin-3-yl)cyclopent-1-en-1-yl)-3-(trifluoroacetamido)benzoate	Rt= 4.30min [MH ⁺] 631
	Ethyl 5-(2-{2-[4-chloro-2-fluorophenyl]methoxy}-5-(trifluoromethyl)pyridin-3-yl)cyclopent-1-en-1-yl)-3-(trifluoroacetamido)benzoate	Rt= 4.29min [MH ⁺] 631

	Ethyl 3-(trifluoroacetamido)-5-(2-{5-(trifluoromethyl)-2-[(2,4,6-trifluorophenyl) methoxy]pyridin-3-yl}cyclopent-1-en-1-yl)-benzoate	Rt= 4.17min [MH ⁺] 633
	Ethyl 3-(trifluoroacetamido)-5-(2-{5-(trifluoromethyl)-2-[(2,4,5-trifluorophenyl) methoxy]pyridin-3-yl}cyclopent-1-en-1-yl)-benzoate	Rt= 4.30min [MH ⁺] 633
	Ethyl 3-(trifluoroacetamido)-5-(2-{5-(trifluoromethyl)-2-[(2,3,6-trifluorophenyl) methoxy]pyridin-3-yl}cyclopent-1-en-1-yl)-benzoate	Rt= 4.26min [MH ⁺] 633
	Ethyl 3-(trifluoroacetamido)-5-[2-(5-[trifluoromethyl]-2-[(4-trifluoromethyl)phenyl]methoxy]pyridin-3-yl)cyclopent-1-en-1-yl]-benzoate	Rt= 4.37min [MH ⁺] 647
	Ethyl 5-[2-(2-{[2-fluoro-4-(trifluoromethyl)phenyl]methoxy}-5-[trifluoromethyl]pyridin-3-yl)cyclopent-1-en-1-yl]-3-(trifluoroacetamido)benzoate	Rt= 4.40min [MH ⁺] 665
	Ethyl 5-(2-{2-[(2-chloro-6-fluorophenyl)methoxy}-5-(trifluoromethyl)pyridin-3-yl)cyclopent-1-en-1-yl]-3-(trifluoroacetamido)benzoate	Rt= 4.32min [MH ⁺] 631

	Ethyl 5-(2-{2-[{(4-bromo-2-fluorophenyl)methoxy]-5-(trifluoromethyl)pyridin-3-yl}cyclopent-1-en-1-yl}-3-(trifluoroacetamido)benzoate 	Rt= 4.39min [MH⁺] 675, 677
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PREPARATION OF EXAMPLES

5 **Example 1 6-{2-[2-[(2,4-Dichlorophenyl)methyl]oxy}-5-(trifluoromethyl)phenyl]-1-cyclopenten-1-yl}-2-pyridinecarboxylic acid**

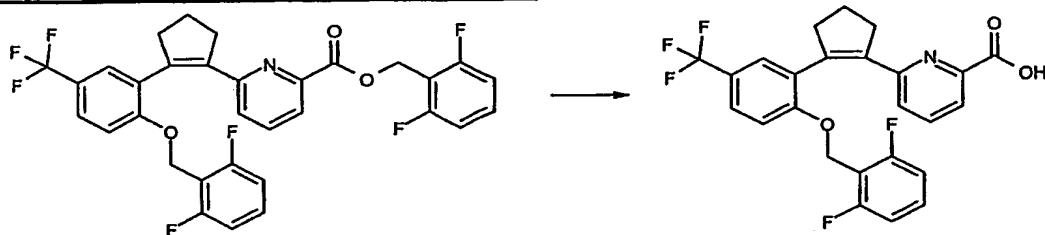


(2,4-Dichlorophenyl)methyl 6-{2-[2-[(2,4-dichlorophenyl)methyl]oxy}-5-(trifluoromethyl)phenyl]-1-cyclopenten-1-yl}-2-pyridinecarboxylate (0.095g), ethanol (2ml)

10 and 2M sodium hydroxide solution were heated in a Smithcreator® microwave to 120°C for 3 minutes. After cooling the reaction was diluted with ethyl acetate and washed with dilute citric acid and brine, dried over MgSO₄, filtered and concentrated in vacuo to yield a yellow oil which was freeze-dried from acetonitrile/H₂O to give the title compound as an off-white solid.

15 ¹H-NMR (CDCl₃) δ: 2.12-2.21 (2H, m), 2.91-2.98 (2H, m), 3.02-3.10 (2H, m), 5.03 (2H, s), 7.04 (1H, d), 7.08-7.16 (2H, m), 7.29 (1H, d), 7.35 (1H, d), 7.41 (1H, d), 7.58 (1H, dd), 7.72 (1H, t), 7.90 (1H, d). LC/MS Rt = 4.50 min, [MH⁺] 508, 510, 512.

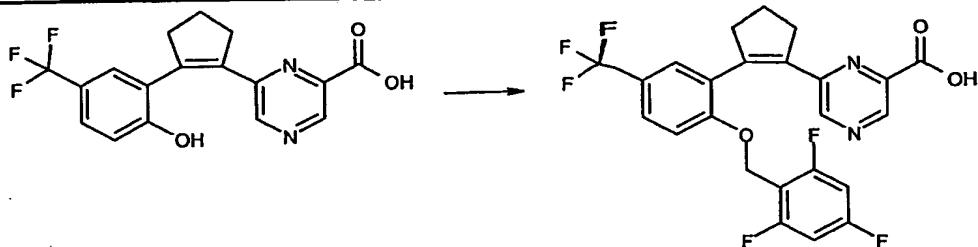
20 **Example 2 6-{2-[2-[(2,6-Difluorophenyl)methyl]oxy}-5-(trifluoromethyl)phenyl]-1-cyclopenten-1-yl}-2-pyridinecarboxylic acid**



Procedure as for 6-{2-[2-[(2,4-dichlorophenyl)methyl]oxy}-5-(trifluoromethyl)phenyl]-1-cyclopenten-1-yl}-2-pyridinecarboxylic acid..

LC/MS t = 3.83, [MH⁺] 476.

Example 3 6-[2-(5-(Trifluoromethyl)-2-{[(2,4,6-trifluorophenyl)methyl]oxy}phenyl)-1-cyclopenten-1-yl]-2-pyrazinecarboxylic acid

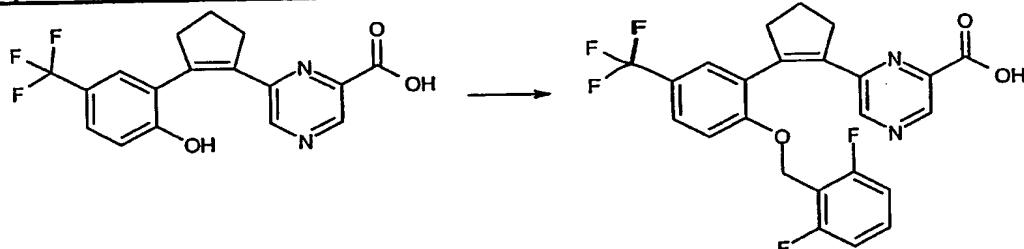


6-[2-Hydroxy-5-(trifluoromethyl)phenyl]-1-cyclopenten-1-yl]-2-pyrazinecarboxylic acid

5 (0.15g, 0.43mmol), 2,4,6-trifluorobenzyl bromide (0.192g, 0.86mmol), potassium carbonate (0.13g, 0.94mmol) and potassium iodide (0.014g, 0.086mmol) were refluxed in methanol (10ml) for 1 hour. The solvent was then removed in vacuo, the residue taken up in ethyl acetate and washed with acidified water (pH3). The aqueous layer was washed with ethyl acetate (x2). The combined organic layers were washed with brine, dried over 10 MgSO₄, filtered and concentrated in vacuo to yield a yellow oil. This was purified by preparative HPLC to yield the title compound as an off-white solid (0.075g).
¹H-NMR (MeOD) δ: 2.02-2.11 (2H, m), 2.85-2.93 (2H, m), 3.01-3.09 (2H, m), 5.04 (2H, s), 6.82 (2H, t), 7.35 (1H, d), 7.44 (1H, s), 7.64 (1H, d), 8.10 (1H, s), 8.86 (1H, s).
LC/MS Rt = 3.90 min, [MH⁺] 495.

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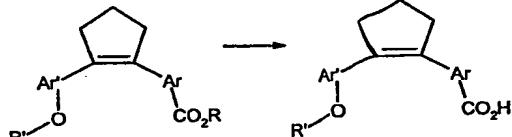
Example 4 6-[2-[2-{[(2,6-Difluorophenyl)methyl]oxy}-5-(trifluoromethyl)phenyl]-1-cyclopenten-1-yl]-2-pyrazinecarboxylic acid



Procedure as for 6-[2-(5-(trifluoromethyl)-2-{[(2,4,6-trifluorophenyl)methyl]oxy}phenyl)-1-cyclopenten-1-yl]-2-pyrazinecarboxylic acid. LC/MS Rt = 3.92 min, [MH⁺] 477.

20

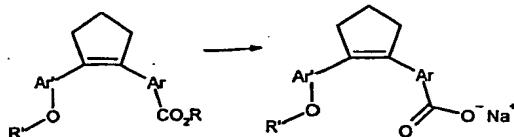
Standard Hydrolysis Procedure A



The ester (0.5mmol) was dissolved in methanol or ethanol (2ml) and 2M sodium hydroxide (1ml) added. The mixture was either stirred at room temperature to reflux for from 30 minutes to 20 hours until the reaction was complete by tlc or heated at 120°C in a Smithcreator® microwave for 3 minutes. The solution was diluted with water then extracted with isohexane or diethyl ether and acidified to pH4 with either hydrochloric acid,

citric acid or acetic acid. The mixture was extracted with diethyl ether or dichloromethane. The organic solution was dried over magnesium sulphate and evaporated to give the title compound.

5 Standard Hydrolysis Procedure B



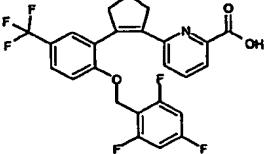
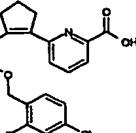
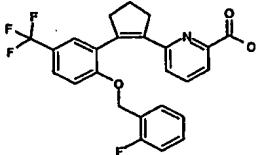
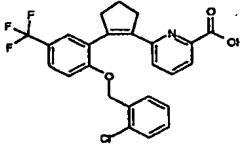
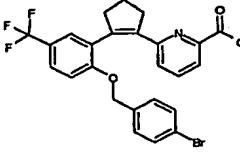
The ester (0.5mmol) was dissolved in methanol or ethanol (2ml) and 2M sodium hydroxide (1ml) added. The mixture was stirred at room temperature to reflux for from 30minutes to 20 hours until the reaction was complete by tlc or heated at 120°C in a Smithcreator® microwave for 3 minutes then evaporated to dryness. The residue was dissolved in water/ethyl acetate or dichloromethane and the organic phase dried (magnesium sulphate), evaporated and the residue either dissolved in a small volume of ether and iso-hexane added to precipitate the salt or dissolved in dioxan and water and freeze-dried.

10

15

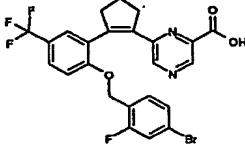
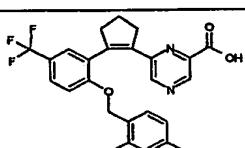
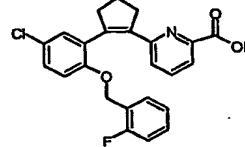
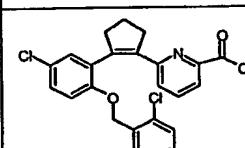
The following Examples were prepared by Standard Hydrolysis Procedure A:

Example	Structure	Name	Data
5		6-{2-[2-[(2,3-Difluorophenyl)methyl]oxy]-5-(trifluoromethyl)phenyl}-1-cyclopenten-1-yl)-2-pyridinecarboxylic acid	LC/MS Rt = 3.91, [MH ⁺] 476
6		6-{2-[2-[(4-Chlorophenyl)methyl]oxy]-5-(trifluoromethyl)phenyl}-1-cyclopenten-1-yl)-2-pyridinecarboxylic acid	LC/MS Rt = 3.97, [MH ⁺] 474, 476

7		6-[2-(5-(Trifluoromethyl)-2-((2,4,6-trifluorophenyl)methyl)oxy)phenyl]-1-cyclopenten-1-yl]-2-pyridinecarboxylic acid	LC/MS Rt = 3.82, [MH ⁺] 494
8		6-[2-{2-[(4-Chloro-2-fluorophenyl)methyl]oxy}-5-(trifluoromethyl)phenyl]-1-cyclopenten-1-yl]-2-pyridinecarboxylic acid	LC/MS Rt = 4.05, [MH ⁺] 492, 494
9		6-[2-{2-[(2-Fluorophenyl)methyl]oxy}-5-(trifluoromethyl)phenyl]-1-cyclopenten-1-yl]-2-pyridinecarboxylic acid	LC/MS Rt = 3.83, [MH ⁺] 458
10		6-[2-{2-[(2-Chlorophenyl)methyl]oxy}-5-(trifluoromethyl)phenyl]-1-cyclopenten-1-yl]-2-pyridinecarboxylic acid	LC/MS Rt = 4.05, [MH ⁺] 474, 476
11		6-[2-{2-[(4-Bromophenyl)methyl]oxy}-5-(trifluoromethyl)phenyl]-1-cyclopenten-1-yl]-2-pyridinecarboxylic acid	LC/MS Rt = 4.08, [MH ⁺] 518, 520.

12		6-{2-[2-[(4-Bromo-2-fluorophenyl)methyl]oxy}-5-(trifluoromethyl)phenyl-1-cyclopenten-1-yl]-2-pyridinecarboxylic acid	LC/MS Rt = 4.13, [MH ⁺] 536, 538.
13		6-{2-[2-[(2-Chloro-4-fluorophenyl)methyl]oxy}-5-(trifluoromethyl)phenyl-1-cyclopenten-1-yl]-2-pyridinecarboxylic acid	LC/MS Rt = 4.07 [MH ⁺] 492, 494.
14		6-{2-[2-[(2-Chloro-6-fluorophenyl)methyl]oxy}-5-(trifluoromethyl)phenyl-1-cyclopenten-1-yl]-2-pyridinecarboxylic acid	LC/MS Rt = 3.93 [MH ⁺] 492, 494
15		6-[2-(5-(Trifluoromethyl)-2-((2,3,6-trifluorophenyl)methyl)oxy)phenyl]-1-cyclopenten-1-yl]-2-pyridinecarboxylic acid	LC/MS Rt = 3.83 [MH ⁺] 494
16		6-{2-[2-[(2-Bromophenyl)methyl]oxy}-5-(trifluoromethyl)phenyl-1-cyclopenten-1-yl]-2-pyridinecarboxylic acid	LC/MS Rt = 4.10 [MH ⁺] 518, 520

17		6-{2-[2-[(4-Fluorophenyl)methyl]oxy]-5-(trifluoromethyl)phenyl}-1-cyclopenten-1-yl}-2-pyrazinecarboxylic acid	LC/MS Rt = 3.93 [MH ⁺] 459.
18		6-{2-[2-[(2,4-Difluorophenyl)methyl]oxy]-5-(trifluoromethyl)phenyl}-1-cyclopenten-1-yl}-2-pyrazinecarboxylic acid	LC/MS Rt = 4.00, [MH ⁺] 477.
19		6-{2-[2-[(4-Chlorophenyl)methyl]oxy]-5-(trifluoromethyl)phenyl}-1-cyclopenten-1-yl}-2-pyrazinecarboxylic acid	LC/MS Rt = 4.08, [MH ⁺] 475, 477
20		6-{2-[2-[(2-Fluorophenyl)methyl]oxy]-5-(trifluoromethyl)phenyl}-1-cyclopenten-1-yl}-2-pyrazinecarboxylic acid	LC/MS Rt = 3.89, [MH ⁺] 459
21		6-{2-[2-[(4-Bromophenyl)methyl]oxy]-5-(trifluoromethyl)phenyl}-1-cyclopenten-1-yl}-2-pyrazinecarboxylic acid	LC/MS Rt = 4.09, [MH ⁺] 517, 519

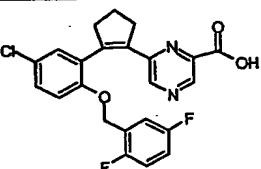
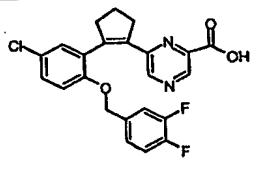
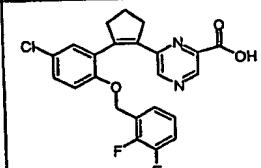
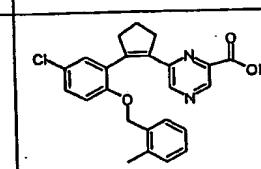
22		6-[2-{[2-[(4-Bromo-2-fluorophenyl)methyl]oxy]-5-(trifluoromethyl)phenyl]-1-cyclopenten-1-yl}-2-pyrazinecarboxylic acid	LC/MS Rt = 4.15, [MH ⁺] 537, 539
23		6-[2-{[2-[(2-Chloro-4-fluorophenyl)methyl]oxy]-5-(trifluoromethyl)phenyl]-1-cyclopenten-1-yl}-2-pyrazinecarboxylic acid	LC/MS Rt = 4.04, [MH ⁺] 493/495
24		6-[2-{(5-Chloro-2-[(2-fluorophenyl)methyl]oxy)phenyl}-1-cyclopenten-1-yl]-2-pyridinecarboxylic acid	¹ H NMR (CDCl ₃) δ: 2.09-2.15 (2H, m), 2.86-2.92 (2H, m), 2.98-3.04 (2H, m), 4.97(2H, s), 6.93-7.02 (3H, m), 7.05-7.11 (2H, m), 7.23-7.27 (3H, m), 7.61-7.72 (1H, bs), 7.86-7.93 (1H, bs). LC/MS Rt = 3.60, [MH ⁺] 424, 426, 427 [MH ⁻] 422, 424
25		6-[2-{(5-Chloro-2-[(2-chloro-4-fluorophenyl)methyl]oxy)phenyl}-1-cyclopenten-1-yl]-2-pyridinecarboxylic acid	¹ H NMR (CDCl ₃) δ: 2.02-2.06 (2H, m), 2.78-2.84 (2H, m), 2.93-2.97 (2H, m), 5.05(2H, s), 6.90 (1H, t), 7.07-7.09 (3H, m), 7.15-7.21(2H, m), 7.21-7.28 (1H, m), 7.63-7.67 (1H, m), 7.86 (1H, d). LC/MS Rt = 3.68, [MH ⁺] 458, 461 [MH ⁻] 456, 459

26		6-[2-(5-Chloro-2-[(2-chlorophenyl)methoxy]phenyl)-1-cyclopenten-1-yl]-2-pyridinecarboxylic acid	¹ H NMR (CDCl ₃) δ: 2.11-2.15 (2H, m), 2.90-2.94 (2H, m), 3.02-3.06 (2H, m), 5.00(2H, s), 6.92 (1H, d), 7.12-7.18 (3H, m), 7.19-7.31(4H, m), 7.69 (1H, t), 7.89 (1H, d). LC/MS Rt = 3.79, [MH ⁺] 440,443 [MH-] 438,441
27		6-[2-(5-Chloro-2-[(2-methylphenyl)methoxy]phenyl)-1-cyclopenten-1-yl]-2-pyridinecarboxylic acid	¹ H NMR (CDCl ₃)δ: 2.07-2.1 (2H, m), 2.85-2.89 (2H, m), 2.98-3.02 (2H, m), 4.8 (2H, s), 6.94 (1H, d), 7.06-7.09 (4H,m), 7.14-7.18(1H,m), 7.23-7.26 (2H,m), 7.64-7.68 (1H, m), 7.87 (1H, d). LC/MS Rt = 3.68, [MH ⁺] 420,422 [MH-] 418,420
28		6-[2-(5-Chloro-2-[(2,6-dichlorophenyl)methoxy]phenyl)-1-cyclopenten-1-yl]-2-pyridinecarboxylic acid	¹ H NMR (CDCl ₃) δ: 2.01-2.05 (2H, m), 2.85-2.87 (2H, m), 2.91-2.95 (2H, m), 5.24(2H, s), 7.09-7.32 (7H,m), 7.63-7.67 (1H, m), 7.86 (1H, d). LC/MS Rt = 3.81, [MH ⁺] 476,478 [MH-] 474,476
29		6-[2-(5-Chloro-2-[(2,4-dimethylphenyl)methoxy]phenyl)-1-cyclopenten-1-yl]-2-pyridinecarboxylic acid	¹ H NMR (CDCl ₃) δ: 2.05-2.11 (2H, m), 2.14 (3H,s), 2.26 (3H,s), 2.85-2.89 (2H, m), 2.97-3.01 (2H, m), 4.85(2H, s), 6.88 (1H, s), 6.92-6.96 (2H,m), 7.08 (1H,s), 7.22-7.26(3H,m), 7.66 (1H, t), 7.87 (1H, d). LC/MS Rt = 3.81, [MH ⁺] 434,436 [MH-] 432,434

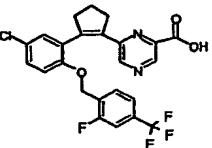
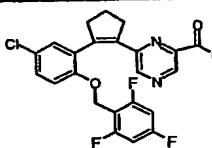
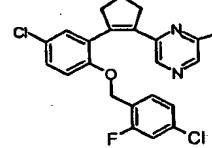
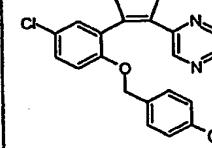
30		6-[2-(5-Chloro-2-[(2,3,6-trifluorophenyl)methyl]oxy)phenyl]-1-cyclopenten-1-yl]-2-pyridinecarboxylic acid	¹ H NMR (CDCl ₃) δ: 2.03-2.11 (2H, m), 2.81-2.85 (2H, m), 2.95-2.99 (2H, m), 5.0(2H, s), 6.73-6.75 (1H, m), 7.03-7.09 (3H, m), 7.25-7.29(2H, m), 7.68 (1H, t), 7.88 (1H, d). LC/MS Rt = 3.60, [MH ⁺] 460,463
31		6-[2-(2-[(4-Bromo-2-fluorophenyl)methyl]oxy)-5-chlorophenyl]-1-cyclopenten-1-yl]-2-pyridinecarboxylic acid	¹ H NMR (CDCl ₃) δ: 2.08-2.13 (2H, m), 2.86-2.89 (2H, m), 2.99-3.03 (2H, m), 4.93(2H, s), 6.93 (1H, d), 6.99 (1H, t), 7.01 (1H, s), 7.14-7.18 (2H,m), 7.25-7.27 (2H, m), 7.71 (1H, t), 7.91 (1H, d). LC/MS Rt = 3.86, [MH ⁺] 504,506 [MH ⁻] 502,503
32		6-[2-(5-Chloro-2-[(2,5-difluorophenyl)methyl]oxy)phenyl]-1-cyclopenten-1-yl]-2-pyridinecarboxylic acid	¹ H NMR (CDCl ₃) δ: 2.13-2.16(2H, m), 2.89-2.93 (2H, m), 3.02-3.07 (2H, m), 4.94(2H, s), 6.78-6.81 (1H, m), 6.90-6.96 (3H, m), 7.14 (1H, bs), 7.25-7.27 (2H, m), 7.69-7.71 (1H, m), 7.86-7.89 (1H, m). LC/MS Rt = 3.86, [MH ⁺] 504,506 [MH ⁻] 502,503
33		6-[2-(5-Chloro-2-[(2-fluorophenyl)methyl]oxy)phenyl]-1-cyclopenten-1-yl]-2-pyrazinecarboxylic acid	¹ H NMR (CDCl ₃) δ: 2.10-2.18(2H, m), 2.91-2.95 (2H, m), 3.02-3.06 (2H, m), 4.94(2H, s), 6.96-7.29 (7H, m), 8.53 (1H,s), 9.04 (1H,s). LC/MS Rt = 4.32, [MH ⁺] 425,427 [MH ⁻] 423,425

34		6-[2-(5-Chloro-2-[(2-chlorophenyl)methyl]oxy)phenyl]-1-cyclopenten-1-yl]-2-pyrazinecarboxylic acid	¹ H NMR (CDCl ₃) δ: 2.12-2.20(2H, m), 2.94-2.97 (2H, m), 3.05-3.08 (2H, m), 4.98 (2H, s), 6.95 (1H, d), 7.12-7.31 (6H, m), 8.55 (1H, s), 9.03(1H,s). LC/MS Rt = 4.65, [MH ⁺] 441,444 [MH ⁻] 439,443
35		6-[2-(5-Chloro-2-[(2-chloro-6-fluorophenyl)methyl]oxy)phenyl]-1-cyclopenten-1-yl]-2-pyrazinecarboxylic acid	¹ H NMR (CDCl ₃) δ: 2.06-2.10(2H, m), 2.85-2.88 (2H, m), 2.96-2.99 (2H, m), 5.02 (2H, s), 6.90 (1H, t, J=8.9 Hz), 7.06-7.12 (2H, m), 7.16-7.2 (2H,m), 7.30 (1H,dd, J=8.8 J=2.6 Hz), 8.48 (1H,s), 9.03(1H,s). LC/MS Rt = 4.40, [MH ⁺] 459,462 [MH ⁻] 457,460
36		6-[2-(5-Chloro-2-[(2,6-dichlorophenyl)methyl]oxy)phenyl]-1-cyclopenten-1-yl]-2-pyrazinecarboxylic acid	¹ H NMR (CDCl ₃) δ: 2.05-2.09(2H, m), 2.85-2.89 (2H, m), 2.94-2.97 (2H, m), 5.11 (2H, s), 7.09 (1H, d, J=8.8 Hz), 7.06-7.12 (2H, m), 7.15-7.32 (5H,m), 8.48 (1H,s), 9.02(1H,s). LC/MS Rt = 4.62, [MH ⁺] 477,479 [MH ⁻] 475,477
37		6-[2-(5-Chloro-2-[(2,4-dichlorophenyl)methyl]oxy)phenyl]-1-cyclopenten-1-yl]-2-pyrazinecarboxylic acid	¹ H NMR(DMSO) δ: 1.97-2.03(2H, m), 2.81-2.85 (2H, m), 2.95-2.98 (2H, m), 5.10 (2H, s), 7.06 (1H, d), 7.17 (1H, d), 7.26 (1H,d), 7.33 (1H,dd), 7.43 (1H, dd), 7.63 (1H, d), 7.80 (1H,s), 8.58(1H,s). LC/MS Rt = 4.92, [MH ⁺] 477,479 [MH ⁻] 475,477

38		6-[2-(5-Chloro-2-[(2,6-difluorophenyl)methyl]oxy)phenyl]-1-cyclopenten-1-yl]-2-pyrazinecarboxylic acid	¹ H NMR(DMSO) δ: 1.89-1.97(2H, m), 2.75-2.79(2H, m), 2.89-2.93 (2H, m), 5.06 (2H, s), 7.03-7.11 (3H, m), 7.30 (1H, d), 7.38-7.47 (2H, m), 7.96(1H,s), 8.75(1H,s). LC/MS Rt = 4.65, [MH+] 443,445 [MH-] 441,443
39		6-[2-(2-[(2-Bromophenyl)methyl]oxy)-5-chlorophenyl]-1-cyclopenten-1-yl]-2-pyrazinecarboxylic acid	¹ H NMR (CDCl ₃) δ: 2.14-2.18(2H, m), 2.94-2.98(2H, m), 3.05-3.09 (2H, m), 4.95 (2H, s), 6.94 (1H, d), 7.11-7.19 (4H, m), 7.27-7.29 (1H, m), 7.48 (1H, d), 8.54(1H,s), 9.03(1H,s). LC/MS Rt = 4.75, [MH+] 487,489 [MH-] 485,487
40		6-[2-(2-[(4-Bromophenyl)methyl]oxy)-5-chlorophenyl]-1-cyclopenten-1-yl]-2-pyrazinecarboxylic acid	¹ H NMR(CDCl ₃) δ: 2.12-2.16(2H, m), 2.91-2.95(2H, m), 3.05-3.09 (2H, m), 4.85 (2H, s), 6.88 (1H, d), 6.99 (2H, d), 7.11 (1H, bs), 7.23-7.25 (1H, m), 7.39 (2H), 8.51(1H,s), 9.04(1H,s). LC/MS Rt = 4.64, [MH+] 487,488 [MH-] 485,487
41		6-[2-(5-Chloro-2-[(2-chloro-4-fluorophenyl)methyl]oxy)phenyl]-1-cyclopenten-1-yl]-2-pyrazinecarboxylic acid	¹ H NMR (CDCl ₃) δ: 2.13-2.17(2H, m), 2.91-2.95(2H, m), 3.05-3.08 (2H, m), 4.94 (2H, s), 6.89-6.95 (2H, m), 7.07 (1H, dd), 7.11-7.15(2H, m), 7.27-7.30 (1H, m), 8.55(1H,s), 9.06(1H,s). LC/MS Rt = 4.59, [MH+] 459,462 [MH-] 457,461

42		6-[2-(5-Chloro-2-[(2,5-difluorophenyl)methyl]oxy)phenyl]-1-cyclopenten-1-yl]-2-pyrazinecarboxylic acid	¹ H NMR (CDCl ₃) δ: 2.12-2.21(2H, m), 2.92-2.98(2H, m), 3.03-3.11 (2H, m), 4.94 (2H, s), 6.78-6.84 (1H, m), 6.91-6.98 (3H, m), 7.15(1H, s), 7.26-7.31 (1H, m), 8.55(1H,s), 9.06(1H,s). LC/MS Rt = 4.29, [MH ⁺] 443,445 [MH-] 441,443
43		6-[2-(5-Chloro-2-[(3,4-difluorophenyl)methyl]oxy)phenyl]-1-cyclopenten-1-yl]-2-pyrazinecarboxylic acid	¹ H NMR (CDCl ₃) δ: 2.15-2.21(2H, m), 2.91-2.97(2H, m), 3.08-3.11 (2H, m), 4.86 (2H, s), 6.81-6.85 (1H, m), 6.89 (1H, d), 6.92-6.97(1H, m), 7.03-7.12 (1H, m), 7.14 (1H, s), 7.26-7.31 (1H,m), 8.58(1H,s), 9.08(1H,s). LC/MS Rt = 4.29, [MH ⁺] 443,445 [MH-] 441,443
44		6-[2-(5-Chloro-2-[(2,3-difluorophenyl)methyl]oxy)phenyl]-1-cyclopenten-1-yl]-2-pyrazinecarboxylic acid	¹ H NMR (CDCl ₃) δ: 2.12-2.19(2H, m), 2.89-2.95(2H, m), 3.03-3.10 (2H, m), 4.98 (2H, s), 6.81-6.87 (1H, m), 6.92-6.97(2H, m), 7.04-7.14 (2H, m), 7.26-7.31 (1H,m), 8.56(1H,s), 9.06(1H,s). LC/MS Rt = 4.34, [MH ⁺] 443,445 [MH-] 441
45		6-[2-(5-Chloro-2-[(2-methylphenyl)methyl]oxy)phenyl]-1-cyclopenten-1-yl]-2-pyrazinecarboxylic acid	¹ H NMR (DMSO) δ: 1.95-2.03(2H, m), 2.19 (3H,s), 2.83-2.86 (2H, m), 2.96-3.0 (2H, m), 5.01 (2H, s), 7.08-7.18 (5H, m), 7.23 (1H, d), 7.36 (1H, dd), 8.03 (1H,s), 8.73 (1H,s). LC/MS Rt = 4.42, [MH ⁺] 421,423 [MH-] 419,421

46		6-[2-(5-Chloro-2-[(4-methylphenyl)methyl]oxy)phenyl]-1-cyclopenten-1-yl]-2-pyrazinecarboxylic acid	¹ H NMR (DMSO) δ: 1.96-2.03(2H, m), 2.25 (3H,s), 2.84-2.86 (2H, m), 2.95-2.99 (2H, m), 4.97 (2H, s), 7.02-7.14 (6H, m), 7.31 (1H, dd, J=8.8, 2.8 Hz), 7.95 (1H,s), 8.69 (1H,s). LC/MS Rt = 4.42, [MH ⁺] 421[MH-] 419,421
47		6-[2-(5-Chloro-2-[(2,4-dimethylphenyl)methyl]oxy)phenyl]-1-cyclopenten-1-yl]-2-pyrazinecarboxylic acid	¹ H NMR (DMSO) δ: 1.91-1.99(2H, m), 2.13 (3H, s), 2.21 (3H, s), 2.83-2.90 (2H, m), 2.96-3.0 (2H, m), 4.94 (2H, s), 6.95-7.04 (3H, m), 7.18-7.24 (2H, m), 7.36-7.40 (1H, m), 8.10 (1H,s), 8.77 (1H,s), 13.65 (1H,s). LC/MS Rt = 4.64, [MH ⁺] 435[MH-] 433,436
48		6-[2-(2-[(4-Bromo-2-fluorophenyl)methyl]oxy)-5-chlorophenyl]-1-cyclopenten-1-yl]-2-pyrazinecarboxylic acid	¹ H NMR (CDCl ₃) δ: 2.12-2.16(2H, m), 2.87-2.91(2H, m), 2.99-3.07 (2H, m), 4.91 (2H, s), 6.93-7.01 (2H, m), 7.12 (1H, bs), 7.18 (1H, d), 7.26-7.29 (1H, m), 8.53 (1H,s), 9.07 (1H,s). LC/MS Rt = 4.64, [MH ⁺] 505,507[MH-] 502,505
49		6-[2-(2-[(2-Bromo-4-fluorophenyl)methyl]oxy)-5-chlorophenyl]-1-cyclopenten-1-yl]-2-pyrazinecarboxylic acid	¹ H NMR (CDCl ₃) δ: 2.13-2.17(2H, m), 2.92-2.96(2H, m), 3.05-3.09 (2H, m), 4.92 (2H, s), 6.92-6.96 (2H, m), 7.10-7.14 (2H, m), 7.24-7.30 (2H, m), 8.54 (1H,s), 9.06 (1H,s). LC/MS Rt = 4.67, [MH ⁺] 505,507[MH-] 503,505

50		6-[2-[5-Chloro-2-((2-fluoro-4-(trifluoromethyl)phenyl)methyl)oxy]phenyl]-1-cyclopenten-1-yl]-2-pyrazinecarboxylic acid	¹ H NMR (DMSO) δ: 1.99-2.03(2H, m), 2.85-2.88(2H, m), 2.97-3.01(2H, m), 5.15 (2H, s), 7.18 (1H, d), 7.23 (1H, d), 7.37 (1H, dd), 7.42 (1H, t), 7.54 (1H, d), 7.63 (1H, d), 8.06 (1H,s), 8.74 (1H,s). LC/MS Rt = 4.46, [MH ⁺] 493,495[MH-] 491,493
51		6-[2-(5-Chloro-2-((2,4,6-trifluorophenyl)methyl)oxy)phenyl]-1-cyclopenten-1-yl]-2-pyrazinecarboxylic acid	¹ H NMR (DMSO) δ: 1.91-1.99(2H, m), 2.78-2.81(2H, m), 2.90-2.94 (2H, m), 4.96 (2H, s), 7.12 (2H, t), 7.21 (1H, d), 7.28 (1H, d), 7.39 (1H, dd), 8.07 (1H,s), 8.81 (1H,s), 13.65 (1H,s). LC/MS Rt = 4.20, [MH ⁺] 461,463[MH-] 459,461
52		6-[2-(5-Chloro-2-((4-chlorophenyl)methyl)oxy)phenyl]-1-cyclopenten-1-yl]-2-pyrazinecarboxylic acid	¹ H NMR (DMSO) δ: 1.96-2.04(2H, m), 2.78-2.83(2H, m), 2.90-2.98 (2H, m), 5.04 (2H, s), 7.12-7.24 (4H, m), 7.32-7.40 (2H, m), 8.07 (1H,s), 8.79 (1H,s). LC/MS Rt = 4.55, [MH ⁺] 459,462[MH-] 457,460
53		6-[2-(5-Chloro-2-((4-chlorophenyl)methyl)oxy)phenyl]-1-cyclopenten-1-yl]-2-pyrazinecarboxylic acid	¹ H NMR (DMSO) δ: 1.91-2.05(2H, m), 2.86-2.90(2H, m), 2.98-3.01 (2H, m), 4.99 (2H, s), 7.12-7.18 (4H, m), 7.33-7.46 (3H, m), 8.06 (1H,s), 8.74 (1H,s). LC/MS Rt = 4.51, [MH ⁺] 441,444[MH-] 439,442

54		6-[2-(5-Chloro-2-[(2,4-dichlorophenyl)methyl]oxy)phenyl]-1-cyclopenten-1-yl]-2-pyridinecarboxylic acid	LC/MS Rt = 4.01, [MH ⁺] 476,478
55		6-[2-(2-[(2-Bromo-4-fluorophenyl)methyl]oxy)-5-chlorophenyl]-1-cyclopenten-1-yl]-2-pyridinecarboxylic acid	LC/MS Rt = 4.01, [MH ⁺] 504,506[MH ⁻] 502,503
56		6-(2-{5-Chloro-2-[(2-methylpropyl)oxy]phenyl}-1-cyclopenten-1-yl)-2-pyridinecarboxylic acid	LC/MS Rt = 3.96, [MH ⁺] 372,374
57		6-(2-{5-Chloro-2-[(cyclopentylmethyl)oxy]phenyl}-1-cyclopenten-1-yl)-2-pyridinecarboxylic acid	LC/MS Rt = 4.26, [MH ⁺] 398,400[MH ⁻] 396,398
58		6-[2-(2-[(4-Fluorophenyl)methyl]oxy)phenyl]-1-cyclopenten-1-yl]-2-pyridinecarboxylic acid	¹ H NMR (DMSO) δ: 1.95-2.03 (2H, m), 2.83-2.87 (2H, m), 2.99-3.33 (2H, m), 5.01 (2H, s), 6.90-6.92 (1H, m), 6.99 (1H, d), 7.04 (1H, dd), 7.09-7.13 (3H, m), 7.22-7.28 (3H, m), 7.58-7.62 (1H, m), 7.74 (1H, d), 12.55-12.95 (1H, br s). LC/MS: Rt = 3.39 min, [M-H] 388, 390.

59		6-[2-(2-[(4-Chlorophenyl)methyl]oxy)phenyl]-1-cyclopenten-1-yl]-2-pyridinecarboxylic acid	¹ H NMR (DMSO) δ: 1.95-2.03 (2H, m), 2.83-2.87 (2H, m), 3.00-3.34 (2H, m), 5.03 (2H, s), 6.89-6.93 (1H, m), 7.00 (1H, d), 7.05 (1H, dd), 7.09 (1H, d), 7.20-7.22 (2H, m), 7.24-7.30 (1H, m), 7.34-7.36 (2H, m), 7.55-7.59 (1H, m), 7.72 (1H, d). LC/MS: Rt = 3.68 min, [M+H] 406.
60		6-[2-(2-[(4-Bromophenyl)methyl]oxy)phenyl]-1-cyclopenten-1-yl]-2-pyridinecarboxylic acid	¹ H NMR (DMSO) δ: 1.96-2.03 (2H, m), 2.83-2.87 (2H, m), 3.00-3.03 (2H, m), 5.01 (2H, s), 6.89-6.93 (1H, m), 6.96 (1H, d), 7.05 (1H, dd), 7.08 (1H, d), 7.15 (2H, d), 7.24-7.28 (1H, m), 7.48 (2H, d), 7.56-7.60 (1H, m), 7.73 (1H), 12.55-12.95 (1H, br s). LC/MS: Rt = 3.77 min, [M+H] 452.
61		6-[2-(2-[(4-Methylphenyl)methyl]oxy)phenyl]-1-cyclopenten-1-yl]-2-pyridinecarboxylic acid	¹ H NMR (DMSO) δ: 1.94-2.01 (2H, m), 2.26 (3H, s), 2.83-2.87 (2H, m), 2.98-3.02 (2H, m), 5.00 (2H, s), 6.86-6.89 (1H, m), 6.92 (1H, d), 7.00 (1H, dd) 7.09-7.11 (5H, m), 7.22-7.26 (1H, m), 7.52-7.55 (1H, m), 7.69 (1H, d, J=7.5Hz). LC/MS: Rt = 3.56 min, [M+H] 386.

62		6-[2-{2-[(4-Trifluoromethyl)phenyl]methyl}oxy]phenyl]-1-cyclopenten-1-yl]-2-pyridinecarboxylic acid	¹ H NMR (DMSO) δ: 1.97-2.05 (2H, m), 2.86-2.89 (2H, m), 3.02-3.05 (2H, m), 5.14 (2H, s), 6.91-6.95 (1H, m), 6.98 (1H, d), 7.07-7.11 (2H, m), 7.25-7.28 (1H, m), 7.41 (2H, d), 7.56-7.60 (1H, m), 7.66 (2H, d), 7.71 (1H, d). LC/MS: Rt = 3.76 min, [M+H] 440.
63		6-[2-(2-Chlorophenyl)methyl]oxyphenyl]-1-cyclopenten-1-yl]-2-pyridinecarboxylic acid	¹ H NMR (DMSO) δ: 1.95-2.02 (2H, m), 2.84-2.88 (2H, m), 3.00-3.03 (2H, m), 5.10 (2H, s), 6.91-6.95 (1H, m), 6.99 (1H, d), 7.04 (1H, dd), 7.14 (1H, d), 7.25-7.32 (4H, m), 7.45 (1H, d), 7.58-7.62 (1H, m), 7.73 (1H, d). LC/MS: Rt = 3.83 min, [M+H] 406.
64		6-[2-(2-Bromophenyl)methyl]oxyphenyl]-1-cyclopenten-1-yl]-2-pyridinecarboxylic acid	¹ H NMR (CDCl ₃) δ: 2.11-2.18 (2H, m), 2.95-2.88 (2H, m), 3.03-3.08 (2H, m), 5.00 (2H, s), 6.99-7.04 (2H, m), 7.09-7.21 (4H, m), 7.28-7.35 (2H, m), 7.49 (1H, dd), 7.64-7.68 (1H, m), 7.86 (1H, d). LC/MS: Rt = 3.77 min, [M+H] 450.
65		6-[2-(2-Methylphenyl)methyl]oxyphenyl]-1-cyclopenten-1-yl]-2-pyridinecarboxylic acid	¹ H NMR (DMSO) δ: 1.93-2.01 (2H, m), 2.23 (3H, s), 2.81-2.84 (2H, m), 2.99-3.02 (2H, m), 5.05 (2H, s), 6.86-6.90 (1H, m), 6.96 (1H, dd), 7.00 (1H, dd), 7.10-7.20 (5H, m), 7.56-7.60 (1H, m), 7.73 (1H, dd), 12.43-13.10 (1H, br s). LC/MS: Rt = 3.64 min, [M+H] 386.

66		6-[2-(2-[(4-Chloro-2-fluorophenyl)methyl]oxy)phenyl]-1-cyclopenten-1-yl]-2-pyridinecarboxylic acid	¹ H NMR (CDCl ₃) δ: 2.08-2.16 (2H, m), 2.90-2.94 (2H, m), 3.00-3.04 (2H, m), 4.98 (2H, s), 6.99-7.03 (3H, m), 7.08-7.13 (2H, m), 7.28-7.31 (3H, m), 7.66-7.70 (1H, m), 7.87 (1H, d, J=7.6Hz). LC/MS: Rt = 3.75 min, [M+H] 424.
67		6-[2-(2-[(4-Bromo-2-fluorophenyl)methyl]oxy)phenyl]-1-cyclopenten-1-yl]-2-pyridinecarboxylic acid	¹ H NMR (DMSO) δ: 1.93-2.01 (2H, m), 2.80-2.84 (2H, m), 2.98-3.01 (2H, m), 5.05 (2H, s), 6.91-6.94 (2H, m), 7.03 (1H, dd), 7.18-7.23 (2H, m), 7.30-7.32 (1H, m), 7.38 (1H, dd), 7.53 (1H, dd), 7.56-7.60 (1H, m), 7.72 (1H, d, J=7.2Hz), 12.56-13.05 (1H, br s). LC/MS: Rt = 3.96 min, [M+H] 470.
68		6-[2-(2-[(2-Fluoro-4-(trifluoromethyl)phenyl)methyl]oxy)phenyl]-1-cyclopenten-1-yl]-2-pyridinecarboxylic acid	¹ H NMR (DMSO) δ: 1.96-2.03 (2H, m), 2.83-2.87 (2H, m), 3.00-3.04 (2H, m), 5.16 (2H, s), 6.93-6.97 (2H, m), 7.07 (1H, d), 7.18 (1H, d), 7.28-7.32 (1H, m), 7.44-7.48 (1H, m), 7.52-7.59 (2H, m), 7.65 (1H, d), 7.70 (1H, d). LC/MS: Rt = 3.98 min, [M+H] 458.
69		6-[2-(2-[(2-Chloro-4-fluorophenyl)methyl]oxy)phenyl]-1-cyclopenten-1-yl]-2-pyridinecarboxylic acid	¹ H NMR (CDCl ₃) δ: 2.10-2.27 (2H, m), 2.92-2.96 (2H, m), 3.02-3.06 (2H, m), 5.00 (2H, s), 6.85-6.90 (1H, m), 6.99-7.07 (3H, m), 7.13 (1H, dd), 7.19-7.21 (1H, m), 7.28-7.34 (2H, m), 7.66-7.70 (1H, m), 7.87 (1H, d). LC/MS: Rt = 3.76 min, [M+H] 424.

70		6-[2-(2-{[(2,4-Dichlorophenyl)methyl]oxy}phenyl)-1-cyclopenten-1-yl]-2-pyridinecarboxylic acid	¹ H NMR (CDCl ₃) δ: 2.10-2.18 (2H, m), 2.93-2.96 (2H, m), 3.02-3.06 (2H, m), 5.00 (2H, s), 6.98-7.04 (2H, m), 7.11-7.17 (3H, m), 7.28-7.34 (3H, m), 7.67-7.71 (1H, m), 7.87 (1H, d). LC/MS: Rt = 4.08 min, [M+H] 440.
71		6-[2-(2-{[(2-Bromo-4-fluorophenyl)methyl]oxy}phenyl)-1-cyclopenten-1-yl]-2-pyridinecarboxylic acid	¹ H NMR (DMSO) δ: 1.94-2.02 (2H, m), 2.83-2.87 (2H, m), 2.99-3.03 (2H, m), 5.02 (2H, s), 6.94-6.99 (2H, m), 7.05 (1H, dd), 7.14 (1H, d), 7.19-7.23 (1H, m), 7.30-7.37 (2H, m), 7.57-7.61 (2H, m), 7.72 (1H, d), 12.56-12.94 (1H, br s). LC/MS: Rt = 3.81 min, [M+H] 468.
72		6-[2-(2-{[(2,4-Dimethylphenyl)methyl]oxy}phenyl)-1-cyclopenten-1-yl]-2-pyridinecarboxylic acid	¹ H NMR (DMSO) δ: 1.92-2.00 (2H, m), 2.18 (3H, s), 2.22 (3H, s), 2.79-2.83 (2H, m), 2.97-3.01 (2H, m), 5.00 (2H, s), 6.87-6.94 (4H, m), 6.98 (1H, dd), 7.06 (1H, d), 7.19 (1H, d), 7.28-7.30 (1H, m), 7.55-7.59 (1H, m), 7.72 (1H, dd), 12.52-12.87 (1H, br s). LC/MS: Rt = 3.70 min, [M-H] 398, 400.

73		6-[2-{2-[(2,4-Bis(trifluoromethyl)phenyl)methyl]oxy}phenyl]-1-cyclopenten-1-yl]-2-pyridinecarboxylic acid	¹ H NMR (DMSO) δ: 1.97-2.05 (2H, m), 2.85-2.89 (2H, m), 3.02-3.06 (2H, m), 5.20 (2H, s), 6.97-7.02 (2H, m), 7.08 (1H, d), 7.14 (1H, dd), 7.27-7.31 (1H, m), 7.58-7.62 (1H, m), 7.66-7.71 (2H, m), 8.02 (1H, d), 12.61-13.05 (1H, br s). LC/MS: Rt = 4.10 min [M+H] 508.
74		6-[2-(2-[(3,4-Difluorophenyl)methyl]oxy)phenyl]-1-cyclopenten-1-yl]-2-pyridinecarboxylic acid	¹ H NMR (DMSO) δ: 1.96-2.04 (2H, m), 2.84-2.88 (2H, m), 3.01-3.04 (2H, m), 5.00 (2H, s), 6.92-6.95 (1H, m), 6.99 (1H, d), 7.07-7.11 (3H, m), 7.15-7.20 (1H, m), 7.26-7.40 (2H, m), 7.58-7.62 (1H, m), 7.73 (1H, d), 12.41-12.98 (1H, br s). LC/MS: Rt = 3.52 min, [M-H] 406, 408.
75		6-[2-(2-[(2,4,6-Trimethylphenyl)methyl]oxy)phenyl]-1-cyclopenten-1-yl]-2-pyridinecarboxylic acid	¹ H NMR (DMSO) δ: 1.84-1.92 (2H, m), 2.18 (9H, s), 2.70-2.74 (2H, m), 2.90-2.94 (2H, m), 4.98 (2H, s), 6.81 (2H, s), 6.90-6.96 (3H, m), 7.31-7.33 (2H, m), 7.56-7.60 (1H, m), 7.71 (1H, dd). LC/MS: Rt = 3.76 min, [M-H] 412, 414.
76		6-[2-(2-[(2,4,5-Trifluorophenyl)methyl]oxy)phenyl]-1-cyclopenten-1-yl]-2-pyridinecarboxylic acid	¹ H NMR (DMSO) δ: 1.94-2.02 (2H, m), 2.81-2.85 (2H, m), 2.98-3.02 (2H, m), 5.02 (2H, s), 6.95-6.97 (2H, m), 7.07 (1H, dd), 7.18 (1H, d), 7.24-7.33 (2H, m), 7.50-7.61 (2H, m), 7.72 (1H, dd), 12.57-12.87 (1H, br s). LC/MS: Rt = 3.58 min, [M+H] 426.

77		6-[2-(2-[(3,4,5-Trifluorophenyl)methyl]oxy)phenyl]-1-cyclopenten-1-yl]-2-pyridinecarboxylic acid	¹ H NMR (DMSO) δ: 1.98-2.05 (2H, m), 2.86-2.89 (2H, m), 3.02-3.06 (2H, m), 4.98 (2H, s), 6.97-7.00 (2H, m), 7.03-7.09 (3H, m), 7.13 (1H, dd), 7.27-7.29 (1H, m), 7.58-7.61 (1H, m), 7.73 (1H, d). LC/MS: Rt = 3.68 min, [M-H] 424, 426.
78		6-(2-{[(Phenylmethyl)oxy]phenyl}-1-cyclopenten-1-yl)-2-pyridinecarboxylic acid	¹ H NMR (DMSO) δ: 1.99-2.06 (2H, m), 2.90-2.94 (2H, m), 2.99-3.02 (2H, m), 5.03 (2H, s), 6.92-6.96 (1H, m), 7.11 (1H, dd), 7.14-7.19 (3H, m), 7.25-7.34 (4H, m), 8.11 (1H, s), 8.80 (1H, s), 13.28-13.89 (1H, br s). LC/MS: Rt = 4.18 min, [M+H] 373.
79		6-[2-(2-[(4-Fluorophenyl)methyl]oxy)phenyl]-1-cyclopenten-1-yl]-2-pyridinecarboxylic acid	¹ H NMR (DMSO) δ: 1.98-2.06 (2H, m), 2.89-2.93 (2H, m), 2.98-3.02 (2H, m), 4.99 (2H, s), 6.93-6.97 (1H, m), 7.08-7.17 (4H, m), 7.20-7.24 (2H, m), 7.30-7.34 (1H, m), 8.09 (1H, s), 8.79 (1H, s), 13.20-13.95 (1H, br s). LC/MS: Rt = 4.16 min, [M-H] 389, 391.
80		6-[2-(2-[(4-Chlorophenyl)methyl]oxy)phenyl]-1-cyclopenten-1-yl]-2-pyridinecarboxylic acid	¹ H NMR (DMSO) δ: 1.99-2.06 (2H, m), 2.89-2.93 (2H, m), 2.93-3.02 (2H, m), 5.01 (2H, s), 6.94-6.97 (1H, m), 7.11-7.15 (2H, m), 7.19 (2H, d), 7.30-7.35 (3H, m), 8.09 (1H, s), 8.80 (1H, s), 13.21-13.89 (1H, br s). LC/MS: Rt = 4.50 min, [M-H] 405, 407.

81		6-[2-(2-{[(2,4-Difluorophenyl)methyl]oxy}phenyl)-1-cyclopenten-1-yl]-2-pyrazinecarboxylic acid	¹ H NMR (DMSO) δ: 1.96-2.03 (2H, m), 2.85-2.89 (2H, m), 2.95-2.99 (2H, m), 5.02 (2H, s), 6.94-7.01 (2H, m), 7.11 (1H, dd), 7.16-7.23 (2H, m), 7.29-7.38 (2H, m), 8.05 (1H, s), 8.78 (1H, s), 13.19-13.78 (1H, br s). LC/MS: Rt = 4.20 min, [M-H] 407, 409.
82		6-[2-(2-{[(2,5-Difluorophenyl)methyl]oxy}phenyl)-1-cyclopenten-1-yl]-2-pyrazinecarboxylic acid	¹ H NMR (DMSO) δ: 1.98-2.05 (2H, m), 2.87-2.91 (2H, m), 2.98-3.01 (2H, m), 5.06 (2H, s), 6.97-7.02 (2H, m), 7.13 (1H, dd), 7.16-7.23 (3H, m), 7.33-7.37 (1H, m), 8.08 (1H, s), 8.78 (1H, s), 13.30-13.78 (1H, br s). LC/MS: Rt = 4.22 min, [M+H] 409.
83		6-[2-(2-{[(2-Fluorophenyl)methyl]oxy}phenyl)-1-cyclopenten-1-yl]-2-pyrazinecarboxylic acid	¹ H NMR (DMSO) δ: 1.96-2.04 (2H, m), 2.86-2.90 (2H, m), 2.96-3.00 (2H, m), 5.01 (2H, s), 6.94-6.98 (1H, m), 7.08-7.28 (5H, m), 7.32-7.34 (2H, m), 8.08 (1H, s), 8.79 (1H, s), 13.20-13.88 (1H, br s). LC/MS: Rt = 4.14 min, [M-H] 389, 391.
84		6-[2-(2-{[(2,4,6-Trifluorophenyl)methyl]oxy}phenyl)-1-cyclopenten-1-yl]-2-pyrazinecarboxylic acid	¹ H NMR (DMSO) δ: 1.91-1.99 (2H, m), 2.79-2.83 (2H, m), 2.91-2.94 (2H, m), 5.01 (2H, s), 6.97-7.00 (1H, m), 7.09-7.15 (3H, m), 7.28 (1H, d), 7.34-7.40 (1H, m), 7.99 (1H, s), 8.78 (1H, s), 13.31-13.79 (1H, br s).

85		5-(2-{5-Chloro-2-[(phenylmethyl)oxy]phenyl}-1-cyclopenten-1-yl)-2-ethyl-3-pyridinecarboxylic acid	¹ H NMR (CDCl ₃) δ: 1.27 (3H, t), 2.05-2.13 (2H, m), 2.86-2.95 (4H, m), 3.15 (2H, q), 4.94 (2H, s), 6.84 (1H, d), 7.05 (1H, d), 7.14-7.19 (2H, m), 7.27-7.32 (4H, m), 8.00 (1H, d), 8.41 (1H, d). LC/MS: Rt = 3.95 min, [M-H] 432, 434.
86		5-[2-(5-Chloro-2-[(4-fluorophenyl)methyl]oxy)phenyl]-1-cyclopenten-1-yl]-2-ethyl-3-pyridinecarboxylic acid	¹ H NMR (CDCl ₃) δ: 1.27 (3H, t), 2.05-2.12 (2H, m), 2.84-2.88 (2H, m), 2.90-2.94 (2H, m), 3.15 (2H, q), 4.87 (2H, s), 6.83 (1H, d), 6.96-7.00 (2H, m), 7.07 (1H, d), 7.11-7.17 (3H, m), 7.99 (1H, d), 8.39 (1H, d). LC/MS: Rt = 3.99 min, [M-H] 450, 452.
87		5-[2-(5-Chloro-2-[(4-chlorophenyl)methyl]oxy)phenyl]-1-cyclopenten-1-yl]-2-ethyl-3-pyridinecarboxylic acid	¹ H NMR (CDCl ₃) δ: 1.27 (3H, t), 2.06-2.13 (2H, m), 2.84-2.88 (2H, m), 2.91-2.95 (2H, m), 3.15 (2H, q), 4.87 (2H, s), 6.81 (1H, d), 7.08-7.10 (2H, m), 7.15 (1H, dd), 7.26-7.28 (3H, m), 7.99 (1H, d), 8.39 (1H, d). LC/MS: Rt = 4.24 min, [M-H] 466, 468.
88		5-{2-[5-Chloro-2-[(4-trifluoromethyl)phenyl]methyl]oxy)phenyl}-1-cyclopenten-1-yl]-2-ethyl-3-pyridinecarboxylic acid	¹ H NMR (CDCl ₃) δ: 1.25 (3H, t), 2.07-2.14 (2H, m), 2.86-2.89 (2H, m), 2.92-2.95 (2H, m), 3.12 (2H, q), 4.96 (2H, s), 6.81 (1H, d), 7.10 (1H, d), 7.16 (1H, dd), 7.26-7.29 (2H, m), 7.55-7.57 (2H, m), 7.97 (1H, d), 8.39 (1H, d). LC/MS: Rt = 4.28 min, [M-H] 500, 502.

89		5-[2-(5-Chloro-2-[(2-fluorophenyl)methyl]oxy)phenyl]-1-cyclopenten-1-yl]-2-ethyl-3-pyridinecarboxylic acid	¹ H NMR (CDCl ₃) δ: 1.13 (3H, t), 1.90-1.97 (2H, m), 2.70-2.80 (2H, m), 2.97-3.02 (2H, m) 4.97 (2H, s), 6.81 (1H, d), 6.93 (1H, d), 6.96-7.03 (2H, m), 7.08 (1H, dd), 7.16-7.21 (2H, m), 7.24 (1H, d), 8.23 (1H, d). LC/MS: Rt = 3.98 min, [M-H] 450, 452.
90		5-[2-(5-Chloro-2-[(2,4-difluorophenyl)methyl]oxy)phenyl]-1-cyclopenten-1-yl]-2-ethyl-3-pyridinecarboxylic acid	¹ H NMR (CDCl ₃) δ: 1.26 (3H, t), 2.05-2.12 (2H, m), 2.82-2.86 (2H, m), 2.90-2.94 (2H, m), 3.14 (2H, q), 4.93 (2H, s), 6.75-6.82 (2H, m), 6.87 (1H, d), 7.07 (1H, d), 7.11-7.15 (1H, m), 7.18 (1H, dd), 7.97 (1H, d), 8.38 (1H, d). LC/MS: Rt = 4.01 min, [M-H] 468, 470.
91		5-[2-(5-Chloro-2-[(2,6-difluorophenyl)methyl]oxy)phenyl]-1-cyclopenten-1-yl]-2-ethyl-3-pyridinecarboxylic acid	¹ H NMR (CDCl ₃) δ: 1.28 (3H, t), 1.99-2.06 (2H, m), 2.76-2.80 (2H, m), 2.84-2.88 (2H, m), 3.16 (2H, q), 5.02 (2H, s), 6.83-6.87 (2H, m), 6.99-7.01 (2H, m), 7.20 (1H, dd), 7.24-7.28 (1H, m), 7.95 (1H, d), 8.34 (1H, d). LC/MS: Rt = 3.90 min, [M-H] 468, 470.
92		5-[2-(5-Chloro-2-[(2-chloro-4-fluorophenyl)methyl]oxy)phenyl]-1-cyclopenten-1-yl]-2-ethyl-3-pyridinecarboxylic acid	¹ H NMR (CDCl ₃) δ: 1.25 (3H, t), 2.07-2.14 (2H, m), 2.85-2.89 (2H, m), 2.93-2.96 (2H, m), 3.14 (2H, q), 4.95 (2H, s), 6.85 (1H, d), 6.90-6.94 (1H, m), 7.07-7.10 (2H, m), 7.17-7.21 (2H, m), 7.99 (1H, d), 8.40 (1H, d). LC/MS: Rt = 4.30 min, [M-H] 484, 486.

93		5-[2-(5-Chloro-2-[(2,4,5-trifluorophenyl)methyl]oxy)phenyl]-1-cyclopenten-1-yl]-2-ethyl-3-pyridinecarboxylic acid	¹ H NMR (CDCl ₃) δ: 1.25 (3H, t), 2.08-2.16 (2H, m), 2.84-2.88 (2H, m), 2.94-2.98 (2H, m), 3.14 (2H, q), 4.90 (2H, s), 6.84-6.92 (2H, m), 6.99-7.05 (1H, m), 7.11 (1H, d), 7.19 (1H, dd), 7.99 (1H, d), 8.39 (1H, d). LC/MS: Rt = 4.13 min, [M-H] 486, 488.
94		5-[2-(5-Chloro-2-[(2,4,6-trifluorophenyl)methyl]oxy)phenyl]-1-cyclopenten-1-yl]-2-ethyl-3-pyridinecarboxylic acid	¹ H NMR (CDCl ₃) δ: 1.28 (3H, t), 2.00-2.07 (2H, m), 2.76-2.80 (2H, m), 2.85-2.89 (2H, m), 3.16 (2H, q), 4.95 (2H, s), 6.60-6.64 (2H, m), 6.97 (1H, d), 7.03 (1H, d), 7.20 (1H, dd), 7.95 (1H, d), 8.35 (1H, d). LC/MS: Rt = 3.98 min, [M-H] 486, 488.
95		3-Methyl-6-{2-[2-[(phenylmethyl)oxy]-5-(trifluoromethyl)phenyl]-1-cyclopenten-1-yl}-2-pyridinecarboxylic acid	¹ H NMR (CDCl ₃) δ: 2.10-2.17 (2H, m), 2.65 (3H, s), 2.91-2.95 (2H, m), 3.00-3.05 (2H, m), 5.00 (2H, s), 7.03 (1H, d), 7.11-7.16 (3H, m), 2.27-2.28 (3H, m), 7.38 (1H, d), 7.44 (1H, d), 7.53 (1H, dd), 1075-11.23 (1H, br s). LC/MS: Rt = 4.10 min, [M-H] 452, 454.
96		6-{2-[2-[(4-Fluorophenyl)methyl]oxy]-5-(trifluoromethyl)phenyl}-1-cyclopenten-1-yl]-3-methyl-2-pyridinecarboxylic acid	¹ H NMR (CDCl ₃) δ: 2.09-2.16 (2H, m), 2.66 (3H, s), 2.89-2.93 (2H, m), 2.99-3.03 (2H, m), 4.97 (2H, s), 6.94-6.98 (2H, m), 7.03 (1H, d), 7.09-7.13 (2H, m), 7.15 (1H, d), 7.37 (1H, d), 7.46 (1H, d), 7.54 (1H, dd), 10.42-11.20 (1H, br s). LC/MS: Rt = 4.06 min, [M-H] 470, 472.

97		6-{2-[2-[(4-Chlorophenyl)methyl]oxy]-5-(trifluoromethyl)phenyl}-1-cyclopenten-1-yl]-3-methyl-2-pyridinecarboxylic acid	¹ H NMR (CDCl ₃) δ: 2.10-2.17 (2H, m), 2.66 (3H, s), 2.90-2.93 (2H, m), 3.00-3.04 (2H, m), 4.97 (2H, s), 7.02 (1H, d), 7.07 (2H, d), 7.16 (1H, d), 7.23-7.25 (2H, m), 7.37 (1H, d), 7.46 (1H, d), 7.54 (1H, dd), 10.50-10.98 (1H, br s). LC/MS: Rt = 4.22 min, [M-H] 486, 488.
98		6-{2-[2-[(2-Fluorophenyl)methyl]oxy]-5-(trifluoromethyl)phenyl}-1-cyclopenten-1-yl]-3-methyl-2-pyridinecarboxylic acid	¹ H NMR (CDCl ₃) δ: 2.09-2.16 (2H, m), 2.65 (3H, s), 2.90-2.94 (2H, m), 3.00-3.04 (2H, m), 5.05 (2H, s), 6.97-7.04 (2H, m), 7.07-7.09 (2H, m), 7.13 (1H, d), 7.25-7.28 (1H, m), 7.39 (1H, d), 7.43 (1H, d), 7.56 (1H, dd), 10.75-11.09 (1H, br s). LC/MS: Rt = 4.07 min, [M-H] 470, 472.
99		6-{2-[2-[(2,4-Difluorophenyl)methyl]oxy]-5-(trifluoromethyl)phenyl}-1-cyclopenten-1-yl]-3-methyl-2-pyridinecarboxylic acid	¹ H NMR (CDCl ₃) δ: 2.08-2.16 (2H, m), 2.66 (3H, s), 2.88-2.91 (2H, m), 2.98-3.03 (2H, m), 5.01 (2H, s), 6.74-6.79 (2H, m), 7.07-7.11 (2H, m), 7.14 (1H, d), 7.38 (1H, d), 7.46 (1H, d), 7.57 (1H, dd), 10.59-11.05 (1H, br s). LC/MS: Rt = 4.10 min, [M-H] 488, 490.
100		6-{2-[2-[(2-Chloro-4-fluorophenyl)methyl]oxy]-5-(trifluoromethyl)phenyl}-1-cyclopenten-1-yl]-3-methyl-2-pyridinecarboxylic acid	¹ H NMR (CDCl ₃) δ: 2.10-2.18 (2H, m), 2.65 (3H, s), 2.90-2.94 (2H, m), 3.01-3.05 (2H, m), 5.04 (2H, s), 6.87-6.91 (1H, m), 7.05-7.09 (2H, m), 7.14-7.18 (2H, m), 7.39 (1H, d), 7.46 (1H, d), 7.57 (1H, dd), 10.56-11.02 (1H, br s). LC/MS: Rt = 4.27 min, [M-H] 504, 506.

101		6-{2-[2-[(2,6-Difluorophenyl)methyl]oxy]-5-(trifluoromethyl)phenyl}-1-cyclopenten-1-yl]-3-methyl-2-pyridinecarboxylic acid	¹ H NMR (CDCl ₃) δ: 2.03-2.10 (2H, m), 2.65 (3H, s), 2.83-2.87 (2H, m), 2.93-2.97 (2H, m), 5.05 (2H, s), 6.79-6.83 (2H, m), 7.08 (1H, d), 7.17 (1H, d), 7.24-7.28 (1H, m), 7.37 (1H, d), 7.41 (1H, d), 7.58 (1H, dd). LC/MS: Rt = 4.03 min, [M-H] 488, 490.
102		6-{2-[2-[(2,3-Difluorophenyl)methyl]oxy]-5-(trifluoromethyl)phenyl}-1-cyclopenten-1-yl]-3-methyl-2-pyridinecarboxylic acid	¹ H NMR (CDCl ₃) δ: 2.09-2.17 (2H, m), 2.65 (3H, s), 2.89-2.93 (2H, m), 3.00-3.04 (2H, m), 5.07 (2H, s), 6.88-6.89 (1H, m), 6.95-7.0 (1H, m), 7.06-7.10 (2H, m), 7.14 (1H, d), 7.40 (1H, d), 7.44 (1H, d), 7.57 (1H, dd), 10.61-10.99 (1H, br s). LC/MS: Rt = 4.10 min, [M-H] 488, 490.
103		6-{2-[2-[(2-Chloro-6-fluorophenyl)methyl]oxy]-5-(trifluoromethyl)phenyl}-1-cyclopenten-1-yl]-3-methyl-2-pyridinecarboxylic acid	¹ H NMR (CDCl ₃) δ: 2.01-2.09 (2H, m), 2.65 (3H, s), 2.83-2.87 (2H, m), 2.92-2.96 (2H, m), 5.11 (1H, d), 6.91-6.97 (1H, m), 7.07 (1H, d), 7.11 (1H, d), 7.19-7.24 (2H, m), 7.37-7.41 (2H, m), 7.59 (1H, dd). LC/MS: Rt = 4.14 min, [M-H] 504, 506.
104		3-Methyl-6-[2-(5-(trifluoromethyl)-2-[(2,4,5-trifluorophenyl)methyl]oxy)phenyl]-1-cyclopenten-1-yl]-2-pyridinecarboxylic acid	¹ H NMR (CDCl ₃) δ: 2.12-2.20 (2H, m), 2.65 (3H, s), 2.89-2.93 (2H, m), 3.02-3.06 (2H, m), 4.99 (2H, s), 6.86-6.93 (2H, m), 7.05 (1H, d), 7.19 (1H, d), 7.41 (1H, d), 7.49 (1H, d), 7.58 (1H, dd), 10.56-10.90 (1H, br s). LC/MS: Rt = 4.15 min, [M-H] 506, 508.

105		3-Methyl-6-[2-(5-(trifluoromethyl)-2-[(2,4,6-trifluorophenyl)methyl]oxy)phenyl]-1-cyclopenten-1-yl]-2-pyridinecarboxylic acid	¹ H NMR (CDCl ₃) δ: 2.03-2.11 (2H, m), 2.66 (3H, s), 2.82-2.86 (2H, m), 2.93-2.98 (2H, m), 5.01 (2H, s), 6.56-6.60 (2H, m), 7.10 (1H, d), 7.17 (1H, d), 7.36 (1H, d), 7.44 (1H, d), 7.58 (1H, dd), 10.56-11.00 (1H, br s). LC/MS: Rt = 4.07 min, [M-H] 506, 508.
106		3-Methyl-6-[2-(5-(trifluoromethyl)-2-[(3,4,5-trifluorophenyl)methyl]oxy)phenyl]-1-cyclopenten-1-yl]-2-pyridinecarboxylic acid	¹ H NMR (CDCl ₃) δ: 2.13-2.21 (2H, m), 2.66 (3H, s), 2.90-2.94 (2H, m), 3.03-3.07 (2H, m), 4.93 (2H, s), 6.73-6.76 (2H, m), 6.97 (1H, d), 7.22 (1H, d), 7.42 (1H, d), 7.51 (1H, d), 7.56 (1H, dd), 10.53-10.80 (1H, br s). LC/MS: Rt = 4.18 min, [M-H] 506, 508.
107		5-[2-(5-Chloro-2-[(2,4-difluorophenyl)methoxy]phenyl)-1-cyclopenten-1-yl]-2-fluorobenzoic acid	LC/MS: Rt = 4.00 min. [M+H] = 476
108		2-(Acetylamino)-5-(2-{5-chloro-2-[(phenylmethyl)oxy]phenyl}-1-cyclopenten-1-yl)benzoic acid	LC/MS: Rt = 4.05 min. [M+H] = 462
109		2-(Acetylamino)-5-[2-(5-chloro-2-[(4-fluorophenyl)methoxy]phenyl)-1-cyclopenten-1-yl]benzoic acid	LC/MS: Rt = 4.04 min. [M+H] = 480

110		2-(Acetylamino)-5-[2-(5-chloro-2-[(2,4-difluorophenyl)methoxy]phenyl)-1-cyclopenten-1-yl]benzoic acid	LC/MS: Rt = 4.06 min. [M+H] = 498
111		2-Amino-5-[2-(5-chloro-2-[(phenylmethyl)oxy]phenyl)-1-cyclopenten-1-yl]benzoic acid	LC/MS: Rt = 3.87 min. [M+H] = 420
112		2-Amino-5-[2-(5-chloro-2-[(4-fluorophenyl)methoxy]phenyl)-1-cyclopenten-1-yl]benzoic acid	LC/MS: Rt = 3.87 min. [M+H] = 438
113		2-Amino-5-[2-(5-chloro-2-[(2,4-difluorophenyl)methoxy]phenyl)-1-cyclopenten-1-yl]benzoic acid	LC/MS: Rt = 3.91 min. [M+H] = 456
114		6-[2-(5-Bromo-2-[(4-fluorophenyl)methoxy]phenyl)-1-cyclopenten-1-yl]-2-pyridinecarboxylic acid	LC/MS: Rt = 3.66 min. [M+H] = 468, 470
115		6-[2-(5-Bromo-2-[(2,4-difluorophenyl)methoxy]phenyl)-1-cyclopenten-1-yl]-2-pyridinecarboxylic acid	LC/MS: Rt = 3.69 min. [M+H] = 486, 488

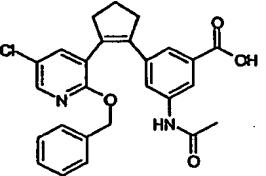
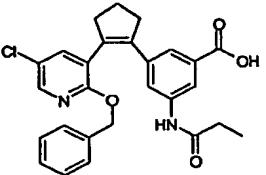
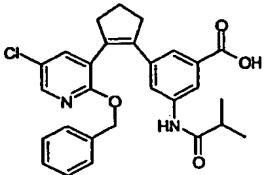
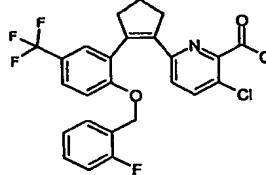
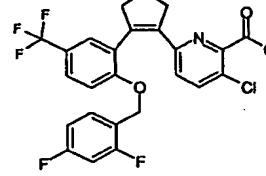
116		6-(2-{5-Bromo-2-[(phenylmethyl)oxy]phenyl}-1-cyclopenten-1-yl)-2-pyridinecarboxylic acid	LC/MS: Rt = 3.65 min. [M+H] = 450,452
117		6-[2-(5-Bromo-2-[(4-methylphenyl)methyl]oxy)phenyl]-1-cyclopenten-1-yl]-2-pyridinecarboxylic acid	LC/MS: Rt = 4.10 min. [M+H] = 464, 466
118		6-[2-(5-Bromo-2-[(4-chlorophenyl)methyl]oxy)phenyl]-1-cyclopenten-1-yl]-2-pyridinecarboxylic acid	LC/MS: Rt = 4.20 min. [M+H] = 484, 486
119		6-[2-(5-Bromo-2-[(2,4,6-trifluorophenyl)methyl]oxy)phenyl]-1-cyclopenten-1-yl]-2-pyridinecarboxylic acid	LC/MS: Rt = 4.07 min. [M+H] = 504,506
120		6-[2-[5-Bromo-2-((2-fluoro-4-(trifluoromethyl)phenyl)methyl)oxy)phenyl]-1-cyclopenten-1-yl]-2-pyridinecarboxylic acid	LC/MS: Rt = 4.36 min. [M+H] = 536,538
121		6-[2-(5-Bromo-2-[(4-bromo-2-fluorophenyl)methyl]oxy)phenyl]-1-cyclopenten-1-yl]-2-pyridinecarboxylic acid	LC/MS: Rt = 4.32 min. [M+H] = 546, 548, 550

122		6-[2-(5-Bromo-2-[(4-chloro-2-fluorophenyl)methyl]oxy)phenyl]-1-cyclopenten-1-yl]-2-pyridinecarboxylic acid	LC/MS: Rt = 4.25 min. [M+H] = 502,504
123		6-[2-(5-Bromo-2-[(4-bromophenyl)methyl]oxy)phenyl]-1-cyclopenten-1-yl]-2-pyridinecarboxylic acid	LC/MS: Rt = 4.26 min. [M+H] = 528, 530, 532
124		6-[2-(5-Bromo-2-[(2-chloro-4-fluorophenyl)methyl]oxy)phenyl]-1-cyclopenten-1-yl]-2-pyridinecarboxylic acid	LC/MS: Rt = 4.35 min. [M+H] = 502,504
125		6-[2-(5-Bromo-2-[(2-fluorophenyl)methyl]oxy)phenyl]-1-cyclopenten-1-yl]-2-pyridinecarboxylic acid	LC/MS: Rt = 4.08 min. [M+H] = 468,470
126		6-[2-(5-Bromo-2-[(2,3,6-trifluorophenyl)methyl]oxy)phenyl]-1-cyclopenten-1-yl]-2-pyridinecarboxylic acid	LC/MS: Rt = 4.05 min. [M+H] = 504, 506
127		6-(2-{5-Bromo-2-[(phenylmethyl)oxy]phenyl}-1-cyclopenten-1-yl)-2-pyrazinecarboxylic acid	LC/MS: Rt = 4.15 min. [M+H] = 451,453

128		6-[2-(5-Bromo-2-[(4-fluorophenyl)methyl]oxy)phenyl]-1-cyclopenten-1-yl]-2-pyrazinecarboxylic acid	LC/MS: Rt = 4.54 min. [M+H] = 469,471
129		6-[2-(5-Bromo-2-[(2,4-difluorophenyl)methyl]oxy)phenyl]-1-cyclopenten-1-yl]-2-pyrazinecarboxylic acid	LC/MS: Rt = 4.57 min. [M+H] = 487, 489
130		6-[2-(5-Bromo-2-[(2,4,6-trifluorophenyl)methyl]oxy)phenyl]-1-cyclopenten-1-yl]-2-pyrazinecarboxylic acid	LC/MS: Rt = 4.47 min. [M+H] = 505, 507
131		6-[2-(5-Bromo-2-[(2-chloro-4-fluorophenyl)methyl]oxy)phenyl]-1-cyclopenten-1-yl]-2-pyrazinecarboxylic acid	LC/MS: Rt = 4.94 min. [M+H] = 503, 505
132		6-[2-(5-Bromo-2-[(4-chloro-2-fluorophenyl)methyl]oxy)phenyl]-1-cyclopenten-1-yl]-2-pyrazinecarboxylic acid	LC/MS: Rt = 4.87 min. [M+H] = 503, 505
133		6-[2-(5-bromo-2-[(4-bromo-2-fluorophenyl)methyl]oxy)phenyl]-1-cyclopenten-1-yl]-2-pyrazinecarboxylic acid	LC/MS: Rt = 4.91 min. [M+H] = 547, 549, 551

134		6-(2-{5-Bromo-2-[{[4-[(trifluoromethyl)oxy]phenyl}methyl]oxy}phenyl)-1-cyclopenten-1-yl]-2-pyrazinecarboxylic acid	LC/MS: Rt = 4.67 min. [M+H] = 535, 537
135		6-[2-(5-Bromo-2-{[(4-chlorophenyl)methyl]oxy}phenyl)-1-cyclopenten-1-yl]-2-pyrazinecarboxylic acid	LC/MS: Rt = 4.77 min. [M+H] = 485, 487
136		6-{2-[5-Bromo-2-({[2-fluoro-4-(trifluoromethyl)phenyl}methyl]oxy}phenyl)-1-cyclopenten-1-yl]-2-pyrazinecarboxylic acid	LC/MS: Rt = 4.69 min. [M+H] = 537, 539
137		6-{2-[5-Bromo-2-({[4-(trifluoromethyl)phenyl}methyl]oxy}phenyl)-1-cyclopenten-1-yl]-2-pyrazinecarboxylic acid	LC/MS: Rt = 4.64 min. [M+H] = 519, 521
138		6-[2-(5-bromo-2-{[(4-bromophenyl)methyl]oxy}phenyl)-1-cyclopenten-1-yl]-2-pyrazinecarboxylic acid	LC/MS: Rt = 4.90 min. [M+H] = 529, 531, 533
139		6-[2-(5-Bromo-2-{[(2E)-3-phenyl-2-propen-1-yl]oxy}phenyl)-1-cyclopenten-1-yl]-2-pyridinecarboxylic acid	¹ H NMR (DMSO) δ: 2.00-2.05(2H, m), 2.67-3.02(4H, br m), 4.50(2H, s), 6.10-6.15(1H, m), 6.5-6.7(1H, m), 6.90-7.10(3H, m), 7.15-7.35(6H, m), 7.50-7.60(1H, m), 7.65-7.70(1H, m).

140		6-{2-[5-Bromo-2-(2-propen-1-yloxy)phenyl]-1-cyclopenten-1-yl}-2-pyridinecarboxylic acid	¹ H NMR (DMSO) δ:1.98-2.04(2H, m), 2.70-2.75(2H, m), 2.95-3.05(2H, m), 4.40(2H, m), 5.10-5.21(2H,m), 5.73-5.76(1H, m), 6.94-6.97(1H, m), 7.05-7.15(2H, m), 7.20-7.25(1H, m), 7.60-7.80(2H,m).
141		6-(2-{5-Bromo-2-[(2-methylpropyl)oxy]phenyl}-1-cyclopenten-1-yl)-2-pyridinecarboxylic acid	LC/MS: Rt = 3.95 min. [M+H] = 416, 418
142		6-{2-[5-Bromo-2-(ethoxy)phenyl]-1-cyclopenten-1-yl}-2-pyridinecarboxylic acid	LC/MS: Rt = 3.44 min. [M+H] = 388, 390
143		6-(2-{5-Bromo-2-[(cyclohexylmethyl)oxy]phenyl}-1-cyclopenten-1-yl)-2-pyridinecarboxylic acid	LC/MS: Rt = 4.41 min. [M+H] = 456, 458
144		6-(2-{5-Bromo-2-[(cyclopentylmethyl)oxy]phenyl}-1-cyclopenten-1-yl)-2-pyridinecarboxylic acid	LC/MS: Rt = 4.25 min. [M+H] = 442, 444
145		3-Amino-5-(2-{5-chloro-2-[(phenylmethyl)oxy]-3-pyridinyl}-1-cyclopenten-1-yl)benzoic acid	LC/MS: Rt = 3.74 min. [M+H] = 421

146		3-(Acetylamino)-5-(2-{5-chloro-2-[(phenylmethyl)oxy]-3-pyridinyl}-1-cyclopenten-1-yl)benzoic acid	LC/MS: Rt = 3.74 min. [M+H] = 463
147		3-(2-{5-Chloro-2-[(phenylmethyl)oxy]-3-pyridinyl}-1-cyclopenten-1-yl)-5-(propanoylamino)benzoic acid	LC/MS: Rt = 3.90 min. [M+H] = 477
148		3-(2-{5-Chloro-2-[(phenylmethyl)oxy]-3-pyridinyl}-1-cyclopenten-1-yl)-5-[(2-methylpropanoyl)amino]benzoic acid	LC/MS: Rt = 4.02 min. [M+H] = 491
149		3-Chloro-6-{2-[2-{[(2-fluorophenyl)methyl]oxy}-5-(trifluoromethyl)phenyl]-1-cyclopenten-1-yl}-2-pyridinecarboxylic acid	LC/MS: Rt = 4.33 min. [M+H] = 492
150		3-Chloro-6-{2-[2-{[(2,4-difluorophenyl)methyl]oxy}-5-(trifluoromethyl)phenyl]-1-cyclopenten-1-yl}-2-pyridinecarboxylic acid	LC/MS: Rt = 4.34 min. [M+H] = 510

151		3-Chloro-6-[2-(5-(trifluoromethyl)-2-((2,4,6-trifluorophenyl)methoxy)phenyl)-1-cyclopenten-1-yl]-2-pyridinecarboxylic acid	LC/MS: Rt = 4.30 min. [M+H] = 528
152		3-Chloro-6-{2-[2-((2,6-difluorophenyl)methoxy)-5-(trifluoromethyl)phenyl]-1-cyclopenten-1-yl}-2-pyridinecarboxylic acid	LC/MS: Rt = 4.31 min. [M+H] = 510
153		3-Chloro-6-{2-[2-((2-chloro-4-fluorophenyl)methoxy)-5-(trifluoromethyl)phenyl]-1-cyclopenten-1-yl}-2-pyridinecarboxylic acid	LC/MS: Rt = 4.54 min. [M+H] = 526
154		3-Chloro-6-{2-[2-((4-chloro-2-fluorophenyl)methoxy)-5-(trifluoromethyl)phenyl]-1-cyclopenten-1-yl}-2-pyridinecarboxylic acid	LC/MS: Rt = 4.55 min. [M+H] = 526

155		3-Chloro-6-{2-[2-((2,4-dichlorophenyl)methoxy)-5-(trifluoromethyl)phenyl]-1-cyclopenten-1-yl}-2-pyridinecarboxylic acid	LC/MS: Rt = 4.77 min. [M+H] = 542, 544
156		3-Chloro-6-{2-[2-((2-fluoro-4-(trifluoromethyl)phenyl)methoxy)-5-(trifluoromethyl)phenyl]-1-cyclopenten-1-yl}-2-pyridinecarboxylic acid	LC/MS: Rt = 4.41 min. [M+H] = 560
157		3-Chloro-6-{2-[2-((phenylmethyl)oxy)-5-(trifluoromethyl)phenyl]-1-cyclopenten-1-yl}-2-pyridinecarboxylic acid	LC/MS: Rt = 4.31 min. [M+H] = 474
158		6-(2-{5-Chloro-4-methyl-2-[(phenylmethyl)oxy]phenyl}-1-cyclopenten-1-yl)-2-pyridinecarboxylic acid	LC/MS: Rt = 3.89 min. [M+H] = 420
159		5-(2-{5-Chloro-2-[(phenylmethyl)oxy]phenyl}-1-cyclopenten-1-yl)-2-methyl-3-pyridinecarboxylic acid	¹ H NMR (DMSO-d ₆) δ: 1.98-2.05 (2H, m), 2.62 (3H, s), 2.79-2.83 (2H, m), 2.87-2.90 (2H, m), 5.03 (2H, s), 7.09-7.33 (8H, m), 7.84 (1H, d), 8.21 (1H, d), 13.1 (1H, s) LC/MS: Rt=3.81 [MH+] 420.4, 422.4

160		5-[2-(5-Chloro-2-[(4-fluorophenyl)methoxy]phenyl)-1-cyclopenten-1-yl]-2-methyl-3-pyridinecarboxylic acid	¹ H NMR (DMSO-d ₆) δ: 1.99-2.06 (2H, m), 2.62 (3H, s), 2.78-2.82 (2H, m), 2.86-2.90 (2H, m), 5.00 (2H, s), 7.10-7.14 (4H, m), 7.20-7.23 (2H, m), 7.31 (1H, dd), 7.81 (1H, d), 8.19 (1H, d), 13.1 (1H,s) LC/MS: Rt=3.85 [MH ⁺] 438.4, 440.4
161		5-[2-(5-Chloro-2-[(2,4-difluorophenyl)methoxy]phenyl)-1-cyclopenten-1-yl]-2-methyl-3-pyridinecarboxylic acid	¹ H NMR (DMSO-d ₆) δ: 1.94-2.02 (2H, m), 2.61 (3H, s), 2.74-2.78 (2H, m), 2.83-2.87 (2H, m), 5.01 (2H, s), 7.02 (1H, dt) 7.10 (1H,d), 7.18-7.35 (4H, m), 7.77 (1H, d), 8.14 (1H, d), 13.1 (1H,s) LC/MS: Rt=3.89 [MH ⁺] 456.3, 458.3
162		5-[2-(5-Chloro-2-[(2,4,5-trifluorophenyl)methoxy]phenyl)-1-cyclopenten-1-yl]-2-methyl-3-pyridinecarboxylic acid	¹ H NMR (DMSO-d ₆) δ: 1.96-2.02 (2H, m), 2.60 (3H, s), 2.77-2.80 (2H, m), 2.85-2.88 (2H, m), 4.98 (2H, s), 7.16 (1H, d), 7.21 (1H, d) 7.21-7.26 (1H, m), 7.35 (1H, dd), 7.47-7.53 (1H, m), 7.75 (1H, d), 8.12 (1H, d), 13.0 (1H,s) LC/MS: Rt=3.86 [MH ⁺] 474.4, 476.4

163		5-[2-(5-Chloro-2-((4-(trifluoromethyl)phenyl)methyl)oxy)phenyl]-1-cyclopenten-1-yl]-2-methyl-3-pyridinecarboxylic acid	¹ H NMR (DMSO-d ₆) δ: 1.99-2.06 (2H, m), 2.60 (3H, s), 2.81-2.85 (2H, m), 2.89-2.93 (2H, m), 5.13 (2H, s), 7.10 (1H, d), 7.14 (1H, d), 7.31-7.38 (3H, m), 7.83 (2H, d), 7.83 (1H, d), 8.21 (1H, d), 13.1 (1H,s) LC/MS: Rt=4.02 [MH ⁺] 488.4, 490.4
164		5-[2-(5-Chloro-2-((4-chlorophenyl)methyl)oxy)phenyl]-1-cyclopenten-1-yl]-2-methyl-3-pyridinecarboxylic acid	¹ H NMR (DMSO-d ₆) δ: 1.96-2.04 (2H, m), 2.62 (3H, s), 2.79-2.82 (2H, m), 2.87-2.91 (2H, m), 5.01 (2H, s), 7.08-7.11 (2H, m), 7.18 (2H, d), 7.29-7.37 (3H, m), 7.82 (1H, d), 8.19 (1H, d), 13.1 (1H,s) LC/MS: Rt=4.02 [MH ⁺] 454.4
165		5-[2-(5-Chloro-2-((2,3,6-trifluorophenyl)methyl)oxy)phenyl]-1-cyclopenten-1-yl]-2-methyl-3-pyridinecarboxylic acid	¹ H NMR (DMSO-d ₆) δ: 1.91-2.01 (2H, m), 2.61 (3H, s), 2.68-2.72 (2H, m), 2.87-2.91 (2H, m), 5.06 (2H, s), 7.07-7.12 (2H, m), 7.27 (1H, d), 7.37 (1H, dd), 7.44-7.53 (1H, m), 7.71 (1H, d), 8.07 (1H, d), 13.1 (1H,s) LC/MS: Rt=3.68 [MH ⁺] 474.6, 476.4

166		5-[2-(5-chloro-2-[(2-chloro-4-fluorophenyl)methyl]oxy)phenyl]-1-cyclopenten-1-yl]-2-methyl-3-pyridinecarboxylic acid	¹ H NMR (DMSO-d ₆) δ: 1.96-2.03 (2H, m), 2.60 (3H, s), 2.77-2.80 (2H, m), 2.85-2.89 (2H, m), 5.01 (2H, s), 7.12-7.20 (3H, m), 7.31-7.35 (2H, m), 7.42 (1H, dd), 7.77 (1H, d), 8.14 (1H, d), 13.1 (1H,s) LC/MS: Rt=4.05 [MH+] 472.4
167		5-[2-(5-Chloro-2-[(2,4,6-trifluorophenyl)methyl]oxy)phenyl]-1-cyclopenten-1-yl]-2-methyl-3-pyridinecarboxylic acid	¹ H NMR (DMSO-d ₆) δ: 1.90-1.97 (2H, m), 2.61 (3H, s), 2.68-2.72 (2H, m), 2.79-2.82 (2H, m), 4.99 (2H, s), 7.09-7.17 (3H, m), 7.26 (1H, d), 7.36 (1H, dd), 7.71 (1H, d), 8.07 (1H, d), 13.1 (1H,s) LC/MS: Rt=3.72 [MH+] 474.4, 476.4
168		5-[2-[5-Chloro-2-({[2-fluoro-4-(trifluoromethyl)phenyl]methyl}oxy)phenyl]-1-cyclopenten-1-yl]-2-methyl-3-pyridinecarboxylic acid	¹ H NMR (DMSO-d ₆) δ: 1.97-2.05 (2H, m), 2.59 (3H, s), 2.78-2.81 (2H, m), 2.87-2.91 (2H, m), 5.14 (2H, s), 7.15 (1H, d), 7.20 (1H, d), 7.34 (1H, dd), 7.42 (1H, t), 7.53 (1H, d), 7.65 (1H, d), 7.78 (1H, d), 8.15 (1H, d), 13.1 (1H,s) LC/MS: Rt=4.05 [MH+] 506.5, 508.4

169		5-[2-(5-Chloro-2-[(4-bromophenyl)methyl]oxyphenyl)-1-cyclopenten-1-yl]-2-methyl-3-pyridinecarboxylic acid	¹ H NMR (DMSO-d ₆) δ: 1.97-2.05 (2H, m), 2.62 (3H, s), 2.79-2.82 (2H, m), 2.87-2.91 (2H, m), 5.00 (2H, s), 7.08-7.13 (4H, m), 7.31 (1H, dd), 7.49 (2H, d), 7.82 (1H, d), 8.19 (1H, d), 13.1 (1H,s) LC/MS: Rt=4.09 [MH ⁺] 500.3, 502.3
170		5-[2-(5-Chloro-2-[(2,6-difluorophenyl)methyl]oxyphenyl)-1-cyclopenten-1-yl]-2-methyl-3-pyridinecarboxylic acid	¹ H NMR (DMSO-d ₆) δ: 1.88-1.96 (2H, m), 2.62 (3H, s), 2.66-2.70 (2H, m), 2.78-2.81 (2H, m), 5.05 (2H, s), 7.05-7.11 (3H, m), 7.26 (1H, d), 7.35 (1H, dd), 7.41-7.48 (1H, m), 7.74 (1H, d), 8.09 (1H, d), 13.1 (1H,s) LC/MS: Rt=3.63 [MH ⁺] 456.5, 458.4
171		5-[2-(5-Chloro-2-[(2-fluorophenyl)methyl]oxyphenyl)-1-cyclopenten-1-yl]-2-methyl-3-pyridinecarboxylic acid	¹ H NMR (DMSO-d ₆) δ: 1.95-2.02 (2H, m), 2.61 (3H, s), 2.75-2.79 (2H, m), 2.84-2.88 (2H, m), 5.07 (2H, s), 7.08-7.24 (5H, m), 7.31-7.37 (2H, m), 7.80 (1H, d), 8.16 (1H, d), 13.1 (1H,s) LC/MS: Rt=3.73 [MH ⁺] 438.5, 440.4

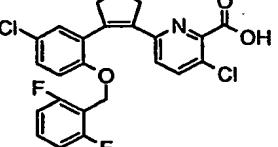
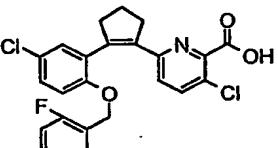
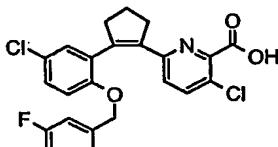
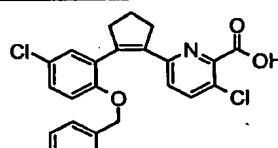
172		2-Methyl-5-{2-[2-[(phenylmethyl)oxy]-5-(trifluoromethyl)phenyl]-1-cyclopenten-1-yl}-3-pyridinecarboxylic acid	¹ H NMR (DMSO-d ₆) δ: 1.99-2.08 (2H, m), 2.61 (3H, s), 2.83-2.87 (2H, m), 2.89-2.92 (2H, m), 5.14 (2H, s), 7.19-7.21 (2H, m), 7.26-7.34 (4H, m), 7.37 (1H, d), 7.63 (1H, dd), 7.82 (1H, d), 8.20 (1H, d), 13.0 (1H,s) LC/MS: Rt=3.72 [MH ⁺] 454.4
173		5-{2-[2-[(4-Fluorophenyl)methyl]oxy}-5-(trifluoromethyl)phenyl]-1-cyclopenten-1-yl}-2-methyl-3-pyridinecarboxylic acid	¹ H NMR (DMSO-d ₆) δ: 1.99-2.07 (2H, m), 2.61 (3H, s), 2.82-2.86 (2H, m), 2.88-2.91 (2H, m), 5.10 (2H, s), 7.11-7.16 (2H, m), 7.22-7.30 (3H, m), 7.38 (1H, d), 7.64 (1H, dd), 7.79 (1H, d), 8.18 (1H, d), 13.0 (1H,s) LC/MS: Rt=3.74 [MH ⁺] 472.4
174		5-{2-[2-[(2,4-Difluorophenyl)methyl]oxy}-5-(trifluoromethyl)phenyl]-1-cyclopenten-1-yl}-2-methyl-3-pyridinecarboxylic acid	¹ H NMR (DMSO-d ₆) δ: 1.96-2.03 (2H, m), 2.60 (3H, s), 2.78-2.82(2H, m), 2.85-2.89 (2H, m), 5.12 (2H, s), 7.04 (1H, dt), 7.22 (1H, dt), 7.32-7.38 (3H, m), 7.65 (1H, dd), 7.74 (1H, d), 8.13 (1H, d), 13.1 (1H,s) LC/MS: Rt=3.78 [MH ⁺] 490.4

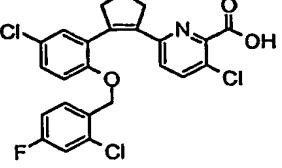
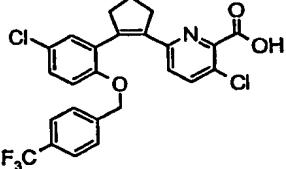
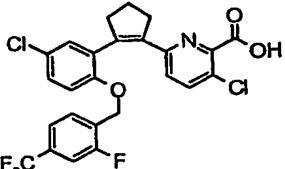
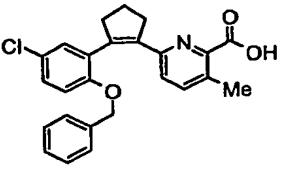
175		5-{2-[2-[(2,4,6-Trifluorophenyl)methoxy]-5-(trifluoromethyl)phenyl]-1-cyclopenten-1-yl}-2-methyl-3-pyridinecarboxylic acid	¹ H NMR (DMSO-d ₆) δ: 1.92-1.99 (2H, m), 2.61 (3H, s), 2.72-2.76(2H, m), 2.80-2.84 (2H, m), 5.09 (2H, s), 7.14-7.19 (2H, m), 7.37 (1H, d), 7.43 (1H, d), 7.67-7.69 (2H, m), 8.07 (1H, d), 13.1 (1H,s) LC/MS: Rt=3.74 [MH ⁺] 508.4
176		5-{2-[2-[(2-Chloro-4-fluorophenyl)methoxy]-5-(trifluoromethyl)phenyl]-1-cyclopenten-1-yl}-2-methyl-3-pyridinecarboxylic acid	¹ H NMR (DMSO-d ₆) δ: 1.97-2.04 (2H, m), 2.59 (3H, s), 2.80-2.84(2H, m), 2.87-2.90 (2H, m), 5.12 (2H, s), 7.19 (1H, dt), 7.35-7.40 (3H, m), 7.45 (1H, dd), 7.66 (1H, dd), 7.75 (1H, d), 8.14 (1H, d), 13.1 (1H,s) LC/MS: Rt=4.00 [MH ⁺] 506.4, 508.4
177		5-{2-[2-[(4-Chloro-2-fluorophenyl)methoxy]-5-(trifluoromethyl)phenyl]-1-cyclopenten-1-yl}-2-methyl-3-pyridinecarboxylic acid	¹ H NMR (DMSO-d ₆) δ: 1.97-2.04 (2H, m), 2.60 (3H, s), 2.79-2.82(2H, m), 2.86-2.90 (2H, m), 5.14 (2H, s), 7.23-7.43 (5H, m), 7.66 (1H, dd), 7.75 (1H, d), 8.14 (1H, d), 13.1 (1H, br s) LC/MS: Rt=3.99 [MH ⁺] 506.4, 508.4

178		5-[2-[2-[(2-Fluorophenyl)methyl]oxy]-5-(trifluoromethyl)phenyl]-1-cyclopenten-1-yl]-2-methyl-3-pyridinecarboxylic acid	¹ H NMR (DMSO-d ₆) δ: 1.97-2.04 (2H, m), 2.61 (3H, s), 2.79-2.83(2H, m), 2.86-2.90 (2H, m), 5.18 (2H, s), 7.13-7.27 (3H, m), 7.35-7.39 (3H, m), 7.65 (1H, dd), 7.78 (1H, d), 8.16 (1H, d), 13.1 (1H, br s) LC/MS: Rt=3.84 [MH ⁺] 472.5
179		2-Methyl-5-[2-(5-(trifluoromethyl)-2-[(2,4,5-trifluorophenyl)methyl]oxy)phenyl]-1-cyclopenten-1-yl]-3-pyridinecarboxylic acid	¹ H NMR (DMSO-d ₆) δ: 1.98-2.05 (2H, m), 2.59 (3H, s), 2.80-2.84(2H, m), 2.87-2.90 (2H, m), 5.09 (2H, s), 7.28-7.31 (1H, dt, m), 7.37 (1H, d), 7.43 (1H, d), 7.51-7.54 (1H, m), 7.67 (1H, dd), 7.73 (1H, d), 8.12 (1H, d), 13.1 (1H,s) LC/MS: Rt=3.95 [MH ⁺] 508.4
180		6-(2-{5-Chloro-2-[(phenylmethyl)oxy]phenyl}-1-cyclopenten-1-yl)-3-(methylthio)-2-pyridinecarboxylic acid	¹ H NMR (DMSO-d ₆) δ: 1.95-2.02 (2H, m), 2.36 (3H, s), 2.82-2.85 (2H, m), 2.97-3.01 (2H, m), 5.02 (2H, s), 7.03 (1H, d), 7.11-7.16 (4H, m), 7.25-7.33 (4H, m), 7.60 (1H, d), 12.6 (1H,s) LC/MS: Rt=4.08 [MH ⁺] 452.4, 454.4

181		6-[2-(5-Chloro-2-[(2-fluorophenyl)methyl]oxy)phenyl]-1-cyclopenten-1-yl]-3-(methylthio)-2-pyridinecarboxylic acid	¹ H NMR (DMSO-d ₆) δ: 1.92-2.00 (2H, m), 2.35 (3H, s), 2.78-2.82(2H, m), 2.95-2.99 (2H, m), 5.07 (2H, s), 7.00 (1H, d), 7.09-7.21 (4H, m), 7.32-7.37 (2H, m), 7.58 (1H, d), 7.79 (1H, d), 12.5 (1H,s) LC/MS: Rt=4.08 [MH ⁺] 470.4, 472.4
182		6-[2-(5-Chloro-2-[(4-fluorophenyl)methyl]oxy)phenyl]-1-cyclopenten-1-yl]-3-(methylthio)-2-pyridinecarboxylic acid	¹ H NMR (DMSO-d ₆) δ: 1.92-2.00 (2H, m), 2.19 (3H, s), 2.74-2.80(2H, m), 2.85-2.92 (2H, m), 5.08 (2H, s), 6.65 (1H, d), 7.08 (1H, d), 7.18-7.23 (4H, m), 7.25-7.41 (3H, m). LC/MS: Rt=4.05 [MH ⁺] 470.4, 472.4
183		6-[2-(5-Chloro-2-[(2,4-difluorophenyl)methyl]oxy)phenyl]-1-cyclopenten-1-yl]-3-(methylthio)-2-pyridinecarboxylic acid	¹ H NMR (DMSO-d ₆) δ: 1.92-1.99 (2H, m), 2.35 (3H, s), 2.77-2.81(2H, m), 2.94-2.98 (2H, m), 5.02 (2H, s), 6.96-7.01 (2H, m), 7.15-7.24 (4H, m), 7.34 (1H, dd), 7.57 (1H, d), 7.79 (1H, d), 12.5 (1H,s) LC/MS: Rt=4.09 [MH ⁺] 488.4, 490.4
184		6-[2-(5-Chloro-2-[(2,4,6-trifluorophenyl)methyl]oxy)phenyl]-1-cyclopenten-1-yl]-3-(methylthio)-2-pyridinecarboxylic acid	¹ H NMR (DMSO-d ₆) δ: 1.87-1.95 (2H, m), 2.36 (3H, s), 2.71-2.74(2H, m), 2.89-2.93 (2H, m), 5.02 (2H, s), 6.91 (1H, d), 7.10-7.14 (3H, m), 7.28 (1H, d), 7.37 (1H, dd), 7.56 (1H, d), 12.5 (1H,s) LC/MS: Rt=4.06 [MH ⁺] 506.3, 508.3

185		3-Chloro-6-(2-{5-chloro-2-[(phenylmethyl)oxy]phenyl}-1-cyclopenten-1-yl)-2-pyridinecarboxylic acid	¹ H NMR (DMSO-d ₆) δ: 1.94-2.01 (2H, m), 2.82-2.86 (2H, m), 2.92-2.96 (2H, m), 5.01 (2H, s), 6.95 (1H, d), 7.10-7.15 (4H, m), 7.26-7.33 (4H, m), 7.74 (1H, d), 13.6 (1H, s) LC/MS: Rt=4.51 [MH ⁺] 440.4
186		3-Chloro-6-[2-(5-chloro-2-[(4-fluorophenyl)methyl]oxy)phenyl]-1-cyclopenten-1-yl]-2-pyridinecarboxylic acid	¹ H NMR (DMSO-d ₆) δ: 1.93-2.01 (2H, m), 2.81-2.84 (2H, m), 2.91-2.95 (2H, m), 4.97 (2H, s), 6.94 (1H, d), 7.09-7.17 (6H, m), 7.32 (1H, dd), 7.74 (1H, d), 13.6 (1H, s) LC/MS: Rt=4.50 [MH ⁺] 458.4
187		3-Chloro-6-[2-(5-chloro-2-[(2-fluorophenyl)methyl]oxy)phenyl]-1-cyclopenten-1-yl]-2-pyridinecarboxylic acid	¹ H NMR (DMSO-d ₆) δ: 1.94-1.99 (2H, m), 2.78-2.82 (2H, m), 2.90-2.94 (2H, m), 5.07 (2H, s), 6.92 (1H, d), 7.11-7.20 (5H, m), 7.32-7.38 (2H, m), 7.73 (1H, d), 13.6 (1H, s) LC/MS: Rt=4.51 [MH ⁺] 458.4
188		3-Chloro-6-[2-(5-chloro-2-[(2,4-difluorophenyl)methyl]oxy)phenyl]-1-cyclopenten-1-yl]-2-pyridinecarboxylic acid	¹ H NMR (DMSO-d ₆) δ: 1.93-1.99 (2H, m), 2.77-2.81 (2H, m), 2.89-2.93 (2H, m), 5.02 (2H, s), 6.90 (1H, d), 7.01 (1H, dt), 7.14-7.26 (4H, m), 7.34 (1H, dd), 7.72 (1H, d), 13.6 (1H, br s) LC/MS: Rt=4.55 [MH ⁺] 476.4

189		3-Chloro-6-[2-(5-chloro-2-{[(2,6-difluorophenyl)methoxy]phenyl}-1-cyclopenten-1-yl)-2-pyridinecarboxylic acid	¹ H NMR (DMSO-d ₆) δ: 1.85-1.93 (2H, m), 2.70-2.73 (2H, m), 2.83-2.87 (2H, m), 5.07 (2H, s), 6.83 (1H, d), 7.05-7.11 (3H, m), 7.27 (1H, d), 7.36-7.47 (2H, m), 7.70 (1H, d), 13.6 (1H, s) LC/MS: Rt=4.43 [MH ⁺] 476.4
190		3-Chloro-6-[2-(5-chloro-2-{[(2,3,6-trifluorophenyl)methoxy]phenyl}-1-cyclopenten-1-yl)-2-pyridinecarboxylic acid	¹ H NMR (DMSO-d ₆) δ: 1.87-1.94 (2H, m), 2.70-2.74 (2H, m), 2.84-2.88 (2H, m), 5.09 (2H, s), 6.84 (1H, d), 7.10-7.15 (2H, m), 7.27 (1H, d), 7.37 (1H, dd), 7.49 (1H, m), 7.71 (1H, d), 13.6 (1H, s) LC/MS: Rt=4.38 [MH ⁺] 494.4
191		3-Chloro-6-[2-(5-chloro-2-{[(2,4,5-trifluorophenyl)methoxy]phenyl}-1-cyclopenten-1-yl)-2-pyridinecarboxylic acid	¹ H NMR (DMSO-d ₆) δ: 1.93-2.01 (2H, m), 2.80-2.83 (2H, m), 2.91-2.94 (2H, m), 4.98 (2H, s), 6.92 (1H, d), 7.18-7.28 (3H, m), 7.35 (1H, dd), 7.50 (1H, m), 7.72 (1H, d), 13.6 (1H, s) LC/MS: Rt=4.48 [MH ⁺] 494.4
192		3-Chloro-6-[2-(5-chloro-2-{[(4-chlorophenyl)methoxy]phenyl}-1-cyclopenten-1-yl)-2-pyridinecarboxylic acid	¹ H NMR (DMSO-d ₆) δ: 1.94-2.01 (2H, m), 2.81-2.85 (2H, m), 2.92-2.96 (2H, m), 4.99 (2H, s), 6.94 (1H, d), 7.08-7.17 (4H, m), 7.30-7.36 (3H, m), 7.72 (1H, d), 13.7 (1H, s) LC/MS: Rt=4.78 [MH ⁺] 476.4

193		3-Chloro-6-[2-(5-chloro-2-[(2-chloro-4-fluorophenyl)methyl]oxy)phenyl]-1-cyclopenten-1-yl]-2-pyridinecarboxylic acid	¹ H NMR (DMSO-d ₆) δ: 1.93-2.00 (2H, m), 2.80-2.83 (2H, m), 2.91-2.95 (2H, m), 5.03 (2H, s), 6.92 (1H, d), 7.15-7.19 (3H, m), 7.25 (1H, dd), 7.34 (1H, dd), 7.43 (1H, dd), 7.73 (1H, d), 13.6 (1H, s) LC/MS: Rt=4.86 [MH ⁺] 494.3
194		3-Chloro-6-{2-[5-chloro-2-({[4-(trifluoromethyl)phenyl]methyl}oxy)phenyl]-1-cyclopenten-1-yl}-2-pyridinecarboxylic acid	¹ H NMR (DMSO-d ₆) δ: 1.94-2.03 (2H, m), 2.83-2.87 (2H, m), 2.94-2.98 (2H, m), 5.10 (2H, s), 6.97 (1H, d), 7.09 (1H, d), 7.20 (1H, d), 7.29-7.35 (4H, m), 7.66 (1H, d), 7.73 (1H, d), 13.6 (1H, s) LC/MS: Rt=4.58 [MH ⁺] 508.4
195		3-Chloro-6-{2-[5-chloro-2-({[2-fluoro-4-(trifluoromethyl)phenyl]methyl}oxy)phenyl]-1-cyclopenten-1-yl}-2-pyridinecarboxylic acid	¹ H NMR (DMSO-d ₆) δ: 1.94-2.02 (2H, m), 2.81-2.84 (2H, m), 2.92-2.96 (2H, m), 5.14 (2H, s), 6.94 (1H, d), 7.17-7.20 (2H, m), 7.32-7.36 (2H, m), 7.53 (1H, d), 7.65 (1H, d), 7.71 (1H, d), 13.6 (1H, s) LC/MS: Rt=4.39 [MH ⁺] 526.3
196		6-(2-{5-Chloro-2-[(phenylmethyl)oxy]phenyl}-1-cyclopenten-1-yl)-3-methyl-2-pyridinecarboxylic acid	¹ H NMR (DMSO-d ₆) δ: 1.94-2.02 (2H, m), 2.38 (3H, s), 2.82-2.85 (2H, m), 2.93-2.99 (2H, m), 5.02 (2H, s), 6.95 (1H, d), 7.10-7.16 (4H, m), 7.26-7.32 (4H, m), 7.50 (1H, d), 12.6 (1H, s) LC/MS: Rt=4.02 [MH ⁺] 420.4, 422.5

197		6-[2-(5-Chloro-2-[(2-fluorophenyl)methyl]oxy)phenyl]-1-cyclopenten-1-yl]-3-methyl-2-pyridinecarboxylic acid	¹ H NMR (DMSO-d ₆) δ: 1.92-1.99 (2H, m), 2.37 (3H, s), 2.78-2.82 (2H, m), 2.93-2.97 (2H, m), 5.07 (2H, s), 6.92 (1H, d), 7.08-7.22 (5H, m), 7.31-7.36 (2H, m), 7.48 (1H, d), 12.6 (1H,s) LC/MS: Rt=4.04 [MH ⁺] 438.4, 440.4
198		6-[2-(5-Chloro-2-[(4-fluorophenyl)methyl]oxy)phenyl]-1-cyclopenten-1-yl]-3-methyl-2-pyridinecarboxylic acid	¹ H NMR (DMSO-d ₆) δ: 1.94-2.01 (2H, m), 2.37 (3H, s), 2.80-2.84 (2H, m), 2.94-2.98 (2H, m), 4.99 (2H, s), 6.93 (1H, d), 7.08-7.19 (6H, m), 7.31, (1H, dd), 7.49 (1H, d), 12.6 (1H,s) LC/MS: Rt=4.04 [MH ⁺] 438.4, 440.4
199		6-[2-(5-Chloro-2-[(2,4-difluorophenyl)methyl]oxy)phenyl]-1-cyclopenten-1-yl]-3-methyl-2-pyridinecarboxylic acid	¹ H NMR (DMSO-d ₆) δ: 1.92-1.99 (2H, m), 2.37 (3H, s), 2.77-2.80 (2H, m), 2.92-2.96 (2H, m), 5.02 (2H, s), 6.91 (1H, d), 7.00 (1H, dt), 7.10 (1H, d), 7.19-7.26 (4H, m), 7.33, (1H, dd), 7.48 (1H, d), 12.6 (1H,s) LC/MS: Rt=4.09 [MH ⁺] 456.4, 458.4
200		6-[2-(5-Chloro-2-[(2,4,5-trifluorophenyl)methyl]oxy)phenyl]-1-cyclopenten-1-yl]-3-methyl-2-pyridinecarboxylic acid	¹ H NMR (DMSO-d ₆) δ: 1.93-2.00 (2H, m), 2.36 (3H, s), 2.79-2.82 (2H, m), 2.93-2.97 (2H, m), 4.99 (2H, s), 6.92 (1H, d), 7.15 (1H, d), 7.19-7.24 (2H, m), 7.34, (1H, dd), 7.47-7.52 (2H, m), 12.6 (1H,s) LC/MS: Rt=4.17 [MH ⁺] 474.4, 476.4

201		6-[2-(5-Chloro-2-[(2,3-difluorophenyl)methoxy]phenyl)-1-cyclopenten-1-yl]-3-methyl-2-pyridinecarboxylic acid	¹ H NMR (DMSO-d ₆) δ: 1.93-2.00 (2H, m), 2.37 (3H, s), 2.78-2.82 (2H, m), 2.93-2.97 (2H, m), 5.11 (2H, s), 6.92 (1H, d), 7.01 (1H, t), 7.10-7.15 (2H, m), 7.20 (1H, d), 7.32-7.37 (2H, m), 7.48 (1H, d), 12.6 (1H, s) LC/MS: Rt=4.09 [MH ⁺] 456.4, 458.4
202		6-[2-(5-Chloro-2-[(3,4,5-trifluorophenyl)methoxy]phenyl)-1-cyclopenten-1-yl]-3-methyl-2-pyridinecarboxylic acid	¹ H NMR (DMSO-d ₆) δ: 1.97-2.04 (2H, m), 2.36 (3H, s), 2.83-2.86 (2H, m), 2.97-3.00 (2H, m), 4.96 (2H, s), 6.95-7.09 (4H, m), 7.19 (1H, d), 7.33, (1H, dd), 7.50 (1H, d), 12.6 (1H, s) LC/MS: Rt=4.24 [MH ⁺] 474.4, 476.4
203		6-[2-(5-Chloro-2-[(2-chloro-6-fluorophenyl)methoxy]phenyl)-1-cyclopenten-1-yl]-3-methyl-2-pyridinecarboxylic acid	¹ H NMR (DMSO-d ₆) δ: 1.85-1.92 (2H, m), 2.38 (3H, s), 2.70-2.73 (2H, m), 2.86-2.89 (2H, m), 5.12 (2H, s), 6.85 (1H, d), 7.02 (1H, d), 7.21, (1H, t), 7.30-7.48 (5H, m), 12.5 (1H, s) LC/MS: Rt=4.24 [MH ⁺] 472.4
204		6-[2-(5-Chloro-2-[(2,4,6-trifluorophenyl)methoxy]phenyl)-1-cyclopenten-1-yl]-3-methyl-2-pyridinecarboxylic acid	¹ H NMR (DMSO-d ₆) δ: 1.87-1.95 (2H, m), 2.38 (3H, s), 2.70-2.74 (2H, m), 2.87-2.91 (2H, m), 5.02 (2H, s), 6.85 (1H, d), 7.07 (1H, d), 7.10-7.16 (2H, m), 7.27 (1H, d), 7.36 (1H, dd), 7.47 (1H, d), 12.6 (1H, s) LC/MS: Rt=4.06 [MH ⁺] 474.4, 476.4

205		6-[2-(5-Chloro-2-[(2,6-difluorophenyl)methoxy]phenyl)-1-cyclopenten-1-yl]-3-methyl-2-pyridinecarboxylic acid	¹ H NMR (DMSO-d ₆) δ: 1.86-1.93 (2H, m), 2.38 (3H, s), 2.70-2.73 (2H, m), 2.87-2.90 (2H, m), 5.08 (2H, s), 6.85 (1H, d), 7.03-7.09 (3H, m), 7.28 (1H, d), 7.34-7.48 (3H, m), 12.6 (1H, s) LC/MS: Rt=3.99 [MH ⁺] 456.4, 458.4
206		6-[2-(5-Chloro-2-[(2-chloro-4-fluorophenyl)methoxy]phenyl)-1-cyclopenten-1-yl]-3-methyl-2-pyridinecarboxylic acid	¹ H NMR (DMSO-d ₆) δ: 1.94-2.00 (2H, m), 2.36 (3H, s), 2.79-2.83 (2H, m), 2.94-2.97 (2H, m), 5.03 (2H, s), 6.91 (1H, d), 7.12-7.20 (3H, m), 7.27-7.34 (2H, m), 7.41 (1H, dd), 7.48 (1H, d), 12.6 (1H, s) LC/MS: Rt=4.31 [MH ⁺] 472.4
207		6-[2-(5-Chloro-2-[(4-chlorophenyl)methoxy]phenyl)-1-cyclopenten-1-yl]-3-methyl-2-pyridinecarboxylic acid	¹ H NMR (DMSO-d ₆) δ: 1.95-2.01 (2H, m), 2.37 (3H, s), 2.81-2.84 (2H, m), 2.95-2.99 (2H, m), 5.00 (2H, s), 6.94 (1H, d), 7.10-7.15 (4H, m), 7.29-7.35 (3H, m), 7.49 (1H, d), 12.6 (1H, s) t=4.26 [MH ⁺] 454.4
208		6-[2-(5-Chloro-2-[(2,4-difluorophenyl)methoxy]phenyl)-1-cyclopenten-1-yl]-3-pyridinecarboxylic acid	¹ H NMR (DMSO-d ₆) δ: 1.92-2.00 (2H, m), 2.79-2.82 (2H, m), 2.94-2.98 (2H, m), 5.00 (2H, s), 6.94 (1H, d), 7.01 (1H, dt), 7.10 (1H, d), 7.15-7.27 (3H, m), 7.34 (1H, dd), 7.92 (1H, dd), 8.86 (1H), 13.2 (1H, s) LC/MS: Rt=4.25 [MH ⁺] 442.3, 444.3

209		2-[2-(5-Chloro-2-[(4,4-difluorophenyl)methoxy]phenyl)-1-cyclopenten-1-yl]-3-pyridinecarboxylic acid	¹ H NMR (DMSO-d ₆) δ: 1.94-2.02 (2H, m), 2.75-2.79 (4H, m), 5.01 (2H, s), 6.73 (1H, d), 6.97 (1H, d), 7.10-7.17 (2H, m), 7.28-7.33 (2H, m), 7.52 (1H, q), 7.98 (1H, dd), 8.56 (1H, dd), 13.0 (1H, s) LC/MS: Rt=3.54 [MH ⁺] 442.3, 444.3
210		2-(2-{5-Chloro-2-[(phenylmethyl)oxy]phenyl}-1-cyclopenten-1-yl)-3-pyridinecarboxylic acid	LC/MS: Rt=3.41 [MH ⁺] 406.4, 408.4
211		2-[2-(5-Chloro-2-[(4-fluorophenyl)methyl]oxy)phenyl]-1-cyclopenten-1-yl]-3-pyridinecarboxylic acid	LC/MS: Rt=3.46 [MH ⁺] 424.3, 426.3
212		2-Ethyl-5-{2-[2-[(phenylmethyl)oxy]-5-(trifluoromethyl)phenyl]-1-cyclopenten-1-yl}-3-pyridinecarboxylic acid	¹ H NMR (DMSO-d ₆) δ: 1.12 (3H, t), 2.00-2.07 (2H, m), 2.83-2.92 (4H, m), 2.98 (2H, q), 5.13 (2H, s), 7.19 (2H, m), 7.27-7.36 (5H, m), 7.63 (1H, dd), 7.79 (1H, d), 8.24 (1H, d), 13.2 (1H, s) LC/MS: Rt=3.87 [MH ⁺] 468.4
213		5-(2-{5-Chloro-2-[(phenylmethyl)oxy]phenyl}-3-pyridinyl)-1-cyclopenten-1-yl)-2-methylbenzoic acid	LC/MS: Rt = 4.04min. [MH ⁺] 420, 422.
214		5-[2-(5-Chloro-2-[(4-fluorophenyl)methyl]oxy)-3-pyridinyl]-1-cyclopenten-1-yl)-2-methylbenzoic acid	LC/MS: Rt = 4.04min. [MH ⁺] 438, 440.

215		5-(2-{5-Chloro-2-[(phenylmethyl)oxy]-3-pyridinyl}-1-cyclopenten-1-yl)-2-fluorobenzoic acid	LC/MS: Rt = 4.44min. [MH ⁺] 424, 426.
216		5-[2-(5-Chloro-2-{[(4-fluorophenyl)methyl]oxy}-3-pyridinyl)-1-cyclopenten-1-yl]-2-fluorobenzoic acid	LC/MS: Rt = 4.39min. [MH ⁺] 442, 444.
217		5-[2-(5-Chloro-2-{[(2-fluorophenyl)methyl]oxy}-3-pyridinyl)-1-cyclopenten-1-yl]-2-fluorobenzoic acid	LC/MS: Rt = 4.32min. [MH ⁺] 442, 444.
218		5-[2-(5-Chloro-2-{[(2,3-difluorophenyl)methyl]oxy}-3-pyridinyl)-1-cyclopenten-1-yl]-2-fluorobenzoic acid	LC/MS: Rt = 4.26min. [MH ⁺] 460, 462.
219		5-[2-(5-Chloro-2-{[(3,4-difluorophenyl)methyl]oxy}-3-pyridinyl)-1-cyclopenten-1-yl]-2-fluorobenzoic acid	LC/MS: Rt = 4.31min. [MH ⁺] 460, 462.
220		5-[2-(5-Chloro-2-{[(2,5-difluorophenyl)methyl]oxy}-3-pyridinyl)-1-cyclopenten-1-yl]-2-fluorobenzoic acid	LC/MS: Rt = 4.32min. [MH ⁺] 460, 462.
221		5-[2-{5-Chloro-2-({[2-fluoro-4-(trifluoromethyl)phenyl]methyl}oxy)-3-pyridinyl}-1-cyclopenten-1-yl]-2-fluorobenzoic acid	LC/MS: Rt = 4.46min. [MH ⁺] 510, 512.

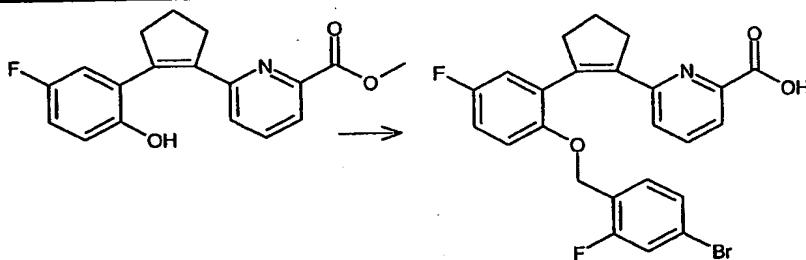
222		5-[2-(5-Chloro-2-[(4-chloro-2-fluorophenyl)methyl]oxy)-3-pyridinyl]-1-cyclopenten-1-yl]-2-fluorobenzoic acid	LC/MS: Rt = 4.53min. [MH ⁺] 476, 477, 478, 479.
223		5-[2-(5-chloro-2-[(2-chloro-4-fluorophenyl)methyl]oxy)-3-pyridinyl]-1-cyclopenten-1-yl]-2-fluorobenzoic acid	LC/MS: Rt = 4.54min. [MH ⁺] 476, 477, 478, 479.
224		5-[2-(5-Chloro-2-[(2,3,4-trifluorophenyl)methyl]oxy)-3-pyridinyl]-1-cyclopenten-1-yl]-2-fluorobenzoic acid	LC/MS: Rt = 4.34min. [MH ⁺] 478, 480.
225		5-[2-(5-Chloro-2-[(2,3,6-trifluorophenyl)methyl]oxy)-3-pyridinyl]-1-cyclopenten-1-yl]-2-fluorobenzoic acid	LC/MS: Rt = 4.26min. [MH ⁺] 478, 480.
226		5-[2-(5-Chloro-2-[(2,4,5-trifluorophenyl)methyl]oxy)-3-pyridinyl]-1-cyclopenten-1-yl]-2-fluorobenzoic acid	LC/MS: Rt = 4.34min. [MH ⁺] 478, 480.
227		5-[2-(5-Chloro-2-[(2,4,6-trifluorophenyl)methyl]oxy)-3-pyridinyl]-1-cyclopenten-1-yl]-2-fluorobenzoic acid	LC/MS: Rt = 4.28min. [MH ⁺] 478, 480.

228		5-[2-(5-Chloro-2-[(3,4,5-trifluorophenyl)methoxy]-3-pyridinyl)-1-cyclopenten-1-yl]-2-fluorobenzoic acid	LC/MS: Rt = 4.29min. [MH ⁺] 478, 480.
229		2-Fluoro-5-(2-[(phenylmethyl)oxy]-3-pyridinyl)-1-cyclopenten-1-yl)benzoic acid	LC/MS: Rt = 4.04min. [MH ⁺] 390.
230		2-Fluoro-5-[2-(2-[(4-fluorophenyl)methyl]oxy)-3-pyridinyl]-1-cyclopenten-1-yl]benzoic acid	LC/MS: Rt=4.06min [MH ⁺] 408.
231		5-[2-(5-Bromo-2-[(4-fluorophenyl)methyl]oxy)-3-pyridinyl)-1-cyclopenten-1-yl]-2-fluorobenzoic acid	LC/MS: Rt = 4.26min. [MH ⁺] 486, 488.
232		5-[2-(5-Bromo-2-[(2-chloro-4-fluorophenyl)methyl]oxy)-3-pyridinyl)-1-cyclopenten-1-yl]-2-fluorobenzoic acid	LC/MS: Rt = 4.25min. [MH ⁺] 520, 522.
233		5-[2-(5-Bromo-2-[(2,4,6-trifluorophenyl)methyl]oxy)-3-pyridinyl)-1-cyclopenten-1-yl]-2-fluorobenzoic acid	LC/MS: Rt = 4.23min. [MH ⁺] 522, 524.
234		5-[2-(5-Bromo-2-[(2-fluorophenyl)methyl]oxy)-3-pyridinyl)-1-cyclopenten-1-yl]-2-fluorobenzoic acid	LC/MS: Rt = 4.38min. [MH ⁺] 486, 488.

235		5-(2-[5-Bromo-2-((2-fluoro-4-(trifluoromethyl)phenyl)methyl)oxy)-3-pyridinyl]-1-cyclopenten-1-yl)-2-fluorobenzoic acid	LC/MS: Rt = 4.54min. [MH ⁺] 554, 556.
236		5-(2-[5-Bromo-2-((phenylmethyl)oxy)-3-pyridinyl]-1-cyclopenten-1-yl)-2-fluorobenzoic acid	LC/MS: Rt=4.42min [MH ⁺] 468, 470.
237		5-[2-(5-Bromo-2-((2,4-difluorophenyl)methyl)oxy)-3-pyridinyl]-1-cyclopenten-1-yl)-2-fluorobenzoic acid	LC/MS: Rt=4.50min [MH ⁺] 504, 506.
238		6-(2-((Phenylmethyl)oxy)-3-pyridinyl)-1-cyclopenten-1-yl)-2-pyridinecarboxylic acid	LC/MS: Rt=3.24min [MH ⁺] 373.
239		3-[2-(5-Bromo-2-((4-fluorophenyl)methyl)oxy)-3-pyridinyl]-1-cyclopenten-1-yl]benzoic acid	LC/MS: Rt = 4.26min [MH ⁺] 468, 470
240		3-[2-(5-Bromo-2-((2,4-difluorophenyl)methyl)oxy)-3-pyridinyl]-1-cyclopenten-1-yl]benzoic acid	LC/MS: Rt = 3.93min [MH ⁺] 486, 488
241		6-{2-[2-(Phenylmethoxy)-5-(trifluoromethyl)pyridin-3-yl]cyclopent-1-en-1-yl}-pyridine-2-carboxylic acid	LC/MS Rt=3.92min [MH ⁺] 441.

242		6-(2-{5-Chloro-2-[(phenylmethyl)oxy]phenyl}-1-cyclopenten-1-yl)-4-pyrimidinecarboxylic acid	LC/MS: Rt=4.88 [MH ⁺] 407.3, 409.3
243		6-[2-(5-Chloro-2-[(2,4-difluorophenyl)methoxy]phenyl)-1-cyclopenten-1-yl]-4-pyrimidinecarboxylic acid	LC/MS: Rt=5.13 [MH ⁺] 443.3, 445.3

Example 244 6-[2-(2-[(4-Bromo-2-fluorophenyl)methoxy]5-fluorophenyl)-1-cyclopenten-1-yl]-2-pyridinecarboxylic acid



5

Methyl 6-[2-(5-fluoro-2-hydroxyphenyl)-1-cyclopenten-1-yl]-2-pyridinecarboxylate (104mg,0.333mmol) was treated with 4-bromo-2-fluorobenzyl bromide (96mg,0.358mmol) and potassium carbonate (140mg,1.0mmol) in 2-butanone (4ml). The reaction mixture was then refluxed overnight under nitrogen, filtered through celite and reduced under vacuum

10 to an oil. The oil was dissolved in methanol (3ml), 2M sodium hydroxide (2ml) was added and the reaction mixture stirred at 65°C for one hour. The reaction mixture was then reduced down to ~1ml under vacuum, diluted to 20ml with water and 2M hydrochloric acid (1.6ml) added as well as a couple of drops of acetic acid to pH~6, extracted with ethyl acetate (2x20ml). The organic extract was then dried over magnesium sulphate, filtered

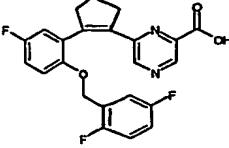
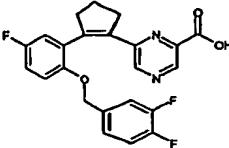
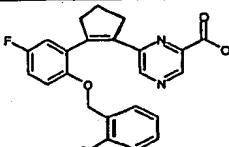
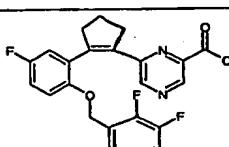
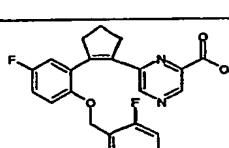
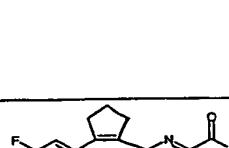
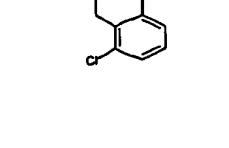
15 and evaporated down to a solid (69mg,42%)

LC/MS Rt=3.94min [MH⁺] 488.

The following Examples were prepared by the procedure used for 6-[2-(2-[(4-bromo-2-fluorophenyl)methyl]oxy)-5-fluorophenyl]-1-cyclopenten-1-yl]-2-pyridinecarboxylic acid:

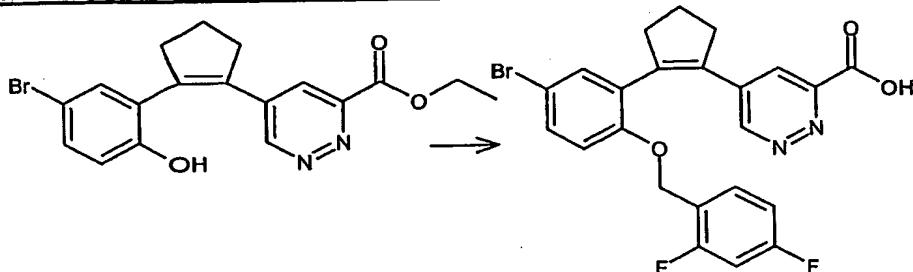
Example		Name	LC/MS
245		6-[2-(2-[(4-bromo-2-fluorophenyl)methyl]oxy)-5-fluorophenyl]-1-cyclopenten-1-yl]-2-pyridinecarboxylic acid	Rt = 4.16, [MH ⁺] 458
246		6-[2-(5-Fluoro-2-[(4-methylphenyl)methyl]oxy)phenyl]-1-cyclopenten-1-yl]-2-pyridinecarboxylic acid	Rt = 3.75, [MH ⁺] 405
247		6-[2-(2-[(4-Chlorophenyl)methyl]oxy)-5-fluorophenyl]-1-cyclopenten-1-yl]-2-pyridinecarboxylic acid	Rt = 4.43, [MH ⁺] 425
248		6-[2-(5-Fluoro-2-[(2,4,6-trifluorophenyl)methyl]oxy)phenyl]-1-cyclopenten-1-yl]-2-pyridinecarboxylic acid	Rt = 4.08, [MH ⁺] 445
249		6-[2-[5-Fluoro-2-((2-fluoro-4-(trifluoromethyl)phenyl)methyl]oxy)phenyl]-1-cyclopenten-1-yl]-2-pyridinecarboxylic acid	Rt = 4.27, [MH ⁺] 475
250		6-[2-(2-[(4-Bromo-2-fluorophenyl)methyl]oxy)-5-fluorophenyl]-1-cyclopenten-1-yl]-2-pyridinecarboxylic acid	Rt = 4.57, [MH ⁺] 489
251		6-[2-(2-[(4-Chloro-2-fluorophenyl)methyl]oxy)-5-fluorophenyl]-1-cyclopenten-1-yl]-2-pyridinecarboxylic acid	Rt = 4.47, [MH ⁺] 443

252		6-[2-(2-[(4-Bromophenyl)methoxy]-5-fluorophenyl)-1-cyclopenten-1-yl]-2-pyrazinecarboxylic acid	Rt = 4.52, [MH ⁺] 471
253		6-[2-(2-[(2-Chloro-4-fluorophenyl)methoxy]-5-fluorophenyl)-1-cyclopenten-1-yl]-2-pyrazinecarboxylic acid	Rt = 4.51, [MH ⁺] 443
254		6-[2-(5-Fluoro-2-[(2-fluorophenyl)methoxy]phenyl)-1-cyclopenten-1-yl]-2-pyrazinecarboxylic acid	Rt = 4.20, [MH ⁺] 409
255		6-[2-(2-[(2,3-Difluorophenyl)methoxy]-5-fluorophenyl)-1-cyclopenten-1-yl]-2-pyrazinecarboxylic acid	Rt = 4.21, [MH ⁺] 427
256		6-[2-(2-[(2,4-Dichlorophenyl)methoxy]-5-fluorophenyl)-1-cyclopenten-1-yl]-2-pyrazinecarboxylic acid	Rt = 4.83, [MH ⁺] 459
257		6-(2-{5-Fluoro-2-[(phenylmethyl)oxy]phenyl}-1-cyclopenten-1-yl)-2-pyrazinecarboxylic acid	Rt = 4.14, [MH ⁺] 391
258		6-[2-(5-Fluoro-2-[(4-fluorophenyl)methoxy]phenyl)-1-cyclopenten-1-yl]-2-pyrazinecarboxylic acid	Rt = 4.12, [MH ⁺] 409
259		6-[2-(2-[(2,4-Difluorophenyl)methoxy]-5-fluorophenyl)-1-cyclopenten-1-yl]-2-pyrazinecarboxylic acid	Rt = 4.15, [MH ⁺] 427

260		6-[2-(2-[(2,5-Difluorophenyl)methyl]oxy)-5-fluorophenyl]-1-cyclopenten-1-yl]-2-pyrazinecarboxylic acid	Rt = 4.13, [MH ⁺] 427
261		6-[2-(2-[(3,4-Difluorophenyl)methyl]oxy)-5-fluorophenyl]-1-cyclopenten-1-yl]-2-pyrazinecarboxylic acid	Rt = 4.14, [MH ⁺] 427
262		6-[2-(2-[(2-Chlorophenyl)methyl]oxy)-5-fluorophenyl]-1-cyclopenten-1-yl]-2-pyrazinecarboxylic acid	Rt = 4.15, [MH ⁺] 425
263		6-[2-(5-Fluoro-2-[(2,3,6-trifluorophenyl)methyl]oxy)phenyl]-1-cyclopenten-1-yl]-2-pyrazinecarboxylic acid	Rt = 4.03, [MH ⁺] 445
264		6-[2-(2-[(2,6-Difluorophenyl)methyl]oxy)-5-fluorophenyl]-1-cyclopenten-1-yl]-2-pyrazinecarboxylic acid	Rt = 5.15, [MH ⁺] 427
265		6-[2-(2-[(2-Chloro-6-fluorophenyl)methyl]oxy)-5-fluorophenyl]-1-cyclopenten-1-yl]-2-pyrazinecarboxylic acid	Rt = 4.19, [MH ⁺] 443
266		6-[2-(2-[(2-Bromophenyl)methyl]oxy)-5-fluorophenyl]-1-cyclopenten-1-yl]-2-pyrazinecarboxylic acid	Rt = 4.51, [MH ⁺] 471

267		6-{2-[5-Fluoro-2-((4-trifluoromethyl)phenyl)methoxy]phenyl}-1-cyclopenten-1-yl}-2-pyridinecarboxylic acid	Rt = 4.25, [MH ⁺] 459
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Example 268 5-[2-(5-Bromo-2-[(2,4-difluorophenyl)methoxy]phenyl)-1-cyclopenten-1-yl]-3-pyridazinecarboxylic acid



5 Ethyl 5-[2-(5-bromo-2-hydroxyphenyl)-1-cyclopenten-1-yl]-3-pyridazinecarboxylate (130mg. 0.333mmol) in dimethylformamide (4ml) was treated with 2,4-difluorobenzyl bromide (80mg, 0.386mmol) and potassium carbonate (200mg, 1.45mmol). The reaction mixture was then stirred at room temperature for 5 hours, filtered through celite, and washed with ethyl acetate (3x15ml). The filtrate was then washed with brine (2x50ml), dried over magnesium sulphate and chromatographed, eluting with 1:1 diethyl ether/isohexane. The product was dissolved in 2M sodium hydroxide (2ml) and methanol (3ml) and heated with stirring for one hour at 70°C. The mixture was evaporated to ~1ml, diluted to 10ml with water and treated with 2M hydrochloric acid (1.8ml) and a couple of drops of acetic acid. The mixture was extracted with ethyl acetate (3x10ml), dried over magnesium sulphate, filtered and evaporated to give the title compound (120mg, 75% yield)

10 LC/MS Rt=4.25 min [MH⁺] 489

15

The following Examples were prepared by the procedure used for 5-[2-(5-bromo-2-[(2,4-difluorophenyl)methoxy]phenyl)-1-cyclopenten-1-yl]-3-pyridazinecarboxylic acid:

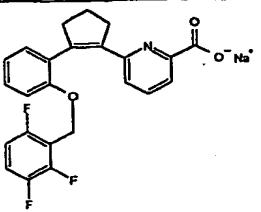
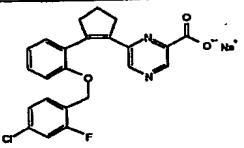
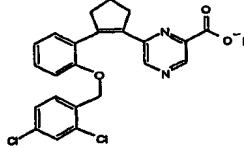
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Example	Structure	Name	¹ H NMR/LCMS
269		5-[2-(5-Bromo-2-((4-fluorophenyl)methoxy)phenyl)-1-cyclopenten-1-yl]-3-pyridazinecarboxylic acid	¹ H NMR (CD ₃ OD) 2.05-2.15(2H,m) 2.85-2.97(4H,m) 4.84(2H,s) 6.93-7.04(3H,m) 7.06-7.13(2H,m) 7.25-7.29(1H,d) 7.40-7.45(1H,dd) 7.83(1H,s) 8.69(1H,s)

270		5-[2-(5-Bromo-2-[(2,6-difluorophenyl)methoxy]phenyl)-1-cyclopenten-1-yl]-3-pyridazinecarboxylic acid	Rt = 4.19, [MH ⁺] 489
271		5-[2-(5-Bromo-2-[(2-fluorophenyl)methoxy]phenyl)-1-cyclopenten-1-yl]-3-pyridazinecarboxylic acid	Rt = 4.29, [MH ⁺] 471
272		5-[2-(5-Bromo-2-[(2,4,6-trifluorophenyl)methoxy]phenyl)-1-cyclopenten-1-yl]-3-pyridazinecarboxylic acid	Rt = 4.19, [MH ⁺] 535
273		5-[2-(5-Bromo-2-[(2,4,5-trifluorophenyl)methoxy]phenyl)-1-cyclopenten-1-yl]-3-pyridazinecarboxylic acid	Rt = 4.30, [MH ⁺] 507
274		5-[2-(5-Bromo-2-[(2,3-difluorophenyl)methoxy]phenyl)-1-cyclopenten-1-yl]-3-pyridazinecarboxylic acid	Rt = 4.27, [MH ⁺] 489
275		5-[2-(5-Bromo-2-[(2-chloro-4-fluorophenyl)methoxy]phenyl)-1-cyclopenten-1-yl]-3-pyridazinecarboxylic acid	Rt = 4.61, [MH ⁺] 505
276		5-[2-(5-Bromo-2-[(phenylmethyl)oxy]phenyl)-1-cyclopenten-1-yl]-3-pyridazinecarboxylic acid	Rt = 4.39, [MH ⁺] 453

The following Examples were prepared by Standard Hydrolysis Procedure B:

Example	Structure	Name	Data
277		Sodium 6-[2-(2-{[(2-bromophenyl)methyl]oxy}-5-chlorophenyl)-1-cyclopenten-1-yl]-2-pyridinecarboxylate	¹ H NMR (DMSO) δ: 1.91-1.97 (2H, m), 2.79-2.83 (2H, m), 2.93-2.98 (2H, m), 5.12 (2H, s), 6.63 (1H, d), 6.96 (1H, s), 7.12 (1H, d), 7.26-7.38 (5H, m), 7.50 (1H, d), 7.64 (1H, d).
278		Sodium 6-[2-(2-{[(2-fluorophenyl)methyl]oxy}phenyl)-1-cyclopenten-1-yl]-2-pyridinecarboxylate	¹ H NMR (CDCl ₃) δ: 1.91-1.98 (2H, m), 2.95-2.98 (2H, m), 5.10 (2H, s), 6.66-6.72 (2H, m), 6.78-6.80 (1H, m), 7.03 (1H, d), 7.08-7.16 (3H, m), 7.29-7.32 (2H, m), 7.38-7.41 (1H, m), 7.60 (1H, d). LC/MS: Rt = 3.38 min, [M+H] 390.
279		Sodium 6-[2-(2-{[(2,4,6-trifluorophenyl)methyl]oxy}phenyl)-1-cyclopenten-1-yl]-2-pyridinecarboxylate	¹ H NMR (DMSO, 50°C) δ: 1.85-1.96 (2H, m), 2.67-2.93 (4H, m), 5.05 (2H, s), 6.69-6.75 (3H, m), 6.95-7.00 (2H, m), 7.09 (1H, d), 7.14-7.18 (1H, m), 7.35-7.40 (1H, m), 7.64 (1H, d). LC/MS: Rt = 3.40 min, [M+H] 426.

280		Sodium 6-[2-(2-[(2,3,6-trifluorophenyl)methyl]oxy)phenyl]-1-cyclopenten-1-yl]-2-pyridinecarboxylate	¹ H NMR (DMSO) δ: 1.86-1.94 (2H, m), 2.70-2.73 (2H, m), 2.88-2.92 (2H, m), 5.24 (2H, s), 6.57 (1H, d), 6.85-6.86 (2H, m), 7.20-7.29 (3H, m), 7.32-7.35 (1H, m), 7.51-7.58 (1H, m), 7.62 (1H, d). LC/MS: Rt = 3.38 min, [M+H] 426.
281		Sodium 6-[2-(2-[(4-chloro-2-fluorophenyl)methyl]oxy)phenyl]-1-cyclopenten-1-yl]-2-pyridinecarboxylate	¹ H NMR (DMSO) δ: 1.94-2.01 (2H, m), 2.80-2.85 (2H, m), 2.95-2.98 (2H, m), 5.12 (2H, s), 6.89-6.94 (1H, m), 6.98 (1H, dd), 7.18 (1H, d), 7.27-7.30 (2H, m), 7.44 (1H, dd), 7.74 (1H, s), 8.55 (1H, s). LC/MS: Rt = 4.48 min, [M-H] 423, 425.
282		Sodium 6-[2-(2-[(2,4-dichlorophenyl)methyl]oxy)phenyl]-1-cyclopenten-1-yl]-2-pyridinecarboxylate	¹ H NMR (DMSO) δ: 1.95-2.03 (2H, m), 2.83-2.87 (2H, m), 2.95-2.99 (2H, m), 5.12 (2H, s), 6.91-6.94 (1H, m), 7.01 (1H, dd), 7.15 (1H, d), 7.28-7.33 (2H, m), 7.43 (1H, dd), 7.63 (1H, d), 7.77 (1H, s), 8.56 (1H, s). LC/MS: Rt = 4.98 min, [M-H] 439, 441.

283		6-(2-{5-Bromo-2-[(phenylmethyl)oxy]phenyl}-1-cyclopenten-1-yl)-3-chloro-2-pyridinecarboxylic acid sodium salt	LC/MS: Rt=4.43, [MH+] 486.3
284		6-[2-(5-Bromo-2-[(4-fluorophenyl)methyl]oxy)phenyl]-1-cyclopenten-1-yl]-3-chloro-2-pyridinecarboxylic acid sodium salt	LC/MS: Rt=4.38 [MH+] 504.3
285		Sodium 6-[2-(5-bromo-2-[(2,4-difluorophenyl)methyl]oxy)phenyl]-1-cyclopenten-1-yl]-3-chloro-2-pyridinecarboxylate	LC/MS: Rt=4.42 [MH+] 522.3
286		Sodium 6-[2-(5-bromo-2-[(2,3,6-trifluorophenyl)methyl]oxy)phenyl]-1-cyclopenten-1-yl]-3-chloro-2-pyridinecarboxylate	LC/MS: Rt=4.27 [MH+] 540.3
287		Sodium 6-[2-(5-bromo-2-[(4-chloro-2-fluorophenyl)methyl]oxy)phenyl]-1-cyclopenten-1-yl]-3-chloro-2-pyridinecarboxylate	LC/MS: Rt=4.65 [MH+] 538.3
288		Sodium 6-[2-(5-bromo-2-[(2,3,4-trifluorophenyl)methyl]oxy)phenyl]-1-cyclopenten-1-yl]-3-chloro-2-pyridinecarboxylate	LC/MS: Rt=4.44 [MH+] 540.3

289		Sodium 5-(2-{5-chloro-2-[(phenylmethyl)oxy]phenyl}-1-cyclopenten-1-yl)-2-(trifluoromethyl)-3-pyridinecarboxylate	LC/MS: Rt=3.37, [MH ⁺] 474.4, 476.3
290		Sodium 5-[2-(5-chloro-2-[(2-fluorophenyl)methoxy]phenyl)-1-cyclopenten-1-yl]-2-(trifluoromethyl)-3-pyridinecarboxylate	LC/MS: Rt=4.30 [MH ⁺] 492.3, 494.3
291		Sodium 5-[2-(5-chloro-2-[(4-fluorophenyl)methoxy]phenyl)-1-cyclopenten-1-yl]-2-(trifluoromethyl)-3-pyridinecarboxylate	LC/MS: Rt=3.83 [MH ⁺] 492.3, 494.3
292		Sodium 5-[2-(5-chloro-2-[(2,4-difluorophenyl)methoxy]phenyl)-1-cyclopenten-1-yl]-2-(trifluoromethyl)-3-pyridinecarboxylate	LC/MS: Rt=4.02 [MH ⁺] 510.3, 512.3
293		Sodium 5-[2-(5-chloro-2-[(2-chloro-4-fluorophenyl)methoxy]phenyl)-1-cyclopenten-1-yl]-2-(trifluoromethyl)-3-pyridinecarboxylate	LC/MS: Rt=4.25 [MH ⁺] 526.3
294		Sodium 5-[2-(5-chloro-2-[(2,6-difluorophenyl)methoxy]phenyl)-1-cyclopenten-1-yl]-2-(trifluoromethyl)-3-pyridinecarboxylate	LC/MS: Rt=4.08 [MH ⁺] 510.3, 512.3

295		Sodium 5-[2-(5-chloro-2-[(4-chloro-2-fluorophenyl)methyl]oxyphenyl)-1-cyclopenten-1-yl]-2-(trifluoromethyl)-3-pyridinecarboxylate	LC/MS: Rt=4.37 [MH+] 526.3
296		Sodium 5-[2-(5-chloro-2-[(2,4,6-trifluorophenyl)methyl]oxyphenyl)-1-cyclopenten-1-yl]-2-(trifluoromethyl)-3-pyridinecarboxylate	LC/MS: Rt=4.15 [MH+] 528.3, 530.3
297		Sodium 5-[2-(5-chloro-2-[(2,4,5-trifluorophenyl)methyl]oxyphenyl)-1-cyclopenten-1-yl]-2-(trifluoromethyl)-3-pyridinecarboxylate	LC/MS: Rt=4.24 [MH+] 528.3, 530.3
298		5-[2-(5-Chloro-2-[(2,4,5-trifluorophenyl)methyl]oxyphenyl)-1-cyclopenten-1-yl]-2-(trifluoromethyl)-3-pyridinecarboxylic acid sodium salt	LC/MS: Rt=4.17 [MH+] 528.3, 530.3
299		Sodium 5-{2-[2-[(phenylmethyl)oxy]-5-(trifluoromethyl)phenyl]-1-cyclopenten-1-yl}-2-(trifluoromethyl)-3-pyridinecarboxylate.	LC/MS: Rt = 3.84min. [M+H] = 508

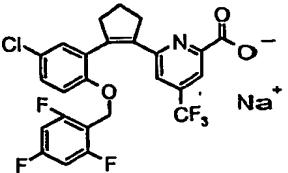
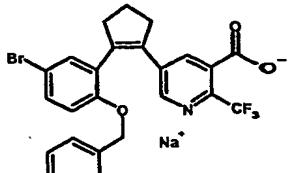
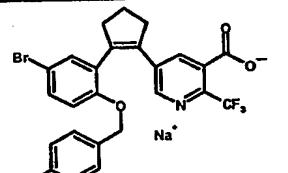
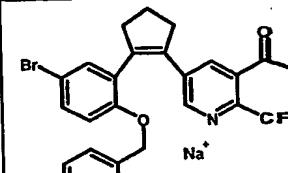
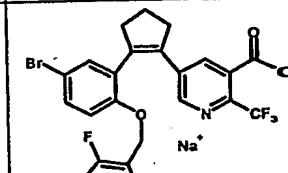
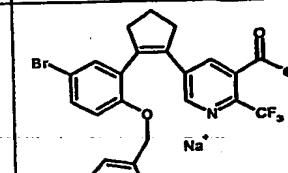
300		5-[2-{2-[(2-fluorophenyl)methyl]oxy}-5-(trifluoromethyl)phenyl]-1-cyclopenten-1-yl]-2-(trifluoromethyl)-3-pyridinecarboxylic acid sodium salt	Rt = 4.23min [M+H] 526
301		5-[2-{2-[(4-fluorophenyl)methyl]oxy}-5-(trifluoromethyl)phenyl]-1-cyclopenten-1-yl]-2-(trifluoromethyl)-3-pyridinecarboxylic acid sodium salt	Rt = 3.77min [M+H] 526
302		5-[2-{2-[(2,4-difluorophenyl)methyl]oxy}-5-(trifluoromethyl)phenyl]-1-cyclopenten-1-yl]-2-(trifluoromethyl)-3-pyridinecarboxylic acid sodium salt	Rt = 4.24min [M+H] 544
303		2-(trifluoromethyl)-5-[2-(5-(trifluoromethyl)-2-[(2,4,6-trifluorophenyl)methyl]oxy)phenyl]-1-cyclopenten-1-yl]-3-pyridinecarboxylic acid sodium salt	Rt = 4.16min [M+H] 562
304		5-[2-{2-[(2-chloro-4-fluorophenyl)methyl]oxy}-5-(trifluoromethyl)phenyl]-1-cyclopenten-1-yl]-2-(trifluoromethyl)-3-pyridinecarboxylic acid sodium salt	Rt = 4.51min [M+H] 560 (1Cl)

305		Sodium 5-{2-[2-{[(4-chloro-2-fluorophenyl)methyl]oxy}-5-(trifluoromethyl)phenyl]-1-cyclopenten-1-yl}-2-(trifluoromethyl)-3-pyridinecarboxylate	Rt = 4.53min [M+H] 560 (1Cl)
306		sodium 6-{2-[2-[(phenylmethyl)oxy]-5-(trifluoromethyl)phenyl]-1-cyclopenten-1-yl}-4-(trifluoromethyl)-2-pyridinecarboxylate	Rt = 3.77min [M+H] 508
307		sodium 6-{2-[2-[(2-fluorophenyl)methyl]oxy}-5-(trifluoromethyl)phenyl]-1-cyclopenten-1-yl}-4-(trifluoromethyl)-2-pyridinecarboxylate	Rt = 4.46min [M+H] 526
308		sodium 6-{2-[2-{[(4-fluorophenyl)methyl]oxy}-5-(trifluoromethyl)phenyl]-1-cyclopenten-1-yl}-4-(trifluoromethyl)-2-pyridinecarboxylate	Rt = 3.74min [M+H] 526
309		sodium 6-{2-[2-{[(2,4-difluorophenyl)methyl]oxy}-5-(trifluoromethyl)phenyl]-1-cyclopenten-1-yl}-4-(trifluoromethyl)-2-pyridinecarboxylate	Rt = 4.43min [M+H] 544

310		sodium 4-(trifluoromethyl)-6-[2-(5-(trifluoromethyl)-2-{[(2,4,6-trifluorophenyl)methyl]oxy}phenyl)-1-cyclopenten-1-yl]-2-pyridinecarboxylate	Rt = 4.36min [M+H] 562
311		sodium 6-{2-[2-[(2-chloro-4-fluorophenyl)methyl]oxy}-5-(trifluoromethyl)phenyl-1-cyclopenten-1-yl]-4-(trifluoromethyl)-2-pyridinecarboxylate	Rt = 4.65min [M+H] 560(1Cl)
312		sodium 6-{2-[2-[(4-chloro-2-fluorophenyl)methyl]oxy}-5-(trifluoromethyl)phenyl-1-cyclopenten-1-yl]-4-(trifluoromethyl)-2-pyridinecarboxylate	Rt = 4.23min [M+H] 560(1Cl)
313		sodium 6-{2-[2-[(3,4-difluorophenyl)methyl]oxy}-5-(trifluoromethyl)phenyl-1-cyclopenten-1-yl]-4-(trifluoromethyl)-2-pyridinecarboxylate	Rt = 4.38min [M+H] 544
314		sodium 6-{2-[2-[(4-bromophenyl)methyl]oxy}-5-(trifluoromethyl)phenyl-1-cyclopenten-1-yl]-4-(trifluoromethyl)-2-pyridinecarboxylate	Rt = 4.50min [M+H] 586,588(1Br)

315		sodium 4-(trifluoromethyl)-6-{2-[5-(trifluoromethyl)-2-((4-(trifluoromethyl)phenyl)methoxy)phenyl]-1-cyclopenten-1-yl}-2-pyridinecarboxylate	Rt = 4.55min [M+H] 576
316		Sodium 6-(2-{5-chloro-2-((phenylmethyl)oxy)phenyl}-1-cyclopenten-1-yl)-4-(trifluoromethyl)-2-pyridinecarboxylate	[M+H] 474.4, 476.4 Rt=4.26min
317		Sodium 6-[2-(5-chloro-2-((2-fluorophenyl)methyl)oxyphenyl)-1-cyclopenten-1-yl]-4-(trifluoromethyl)-2-pyridinecarboxylate	[M+H] 492.4, 494.4 Rt=3.85min
318		Sodium 6-[2-(5-chloro-2-((4-fluorophenyl)methyl)oxyphenyl)-1-cyclopenten-1-yl]-4-(trifluoromethyl)-2-pyridinecarboxylate	[M+H] 492.3, 494.3 Rt=4.53min
319		Sodium 6-[2-(5-chloro-2-((2,4-difluorophenyl)methyl)oxyphenyl)-1-cyclopenten-1-yl]-4-(trifluoromethyl)-2-pyridinecarboxylate	[M+H] 510.3, 512.3 Rt=4.50min
320		Sodium 6-[2-(5-chloro-2-((2,4,5-trifluorophenyl)methyl)oxyphenyl)-1-cyclopenten-1-yl]-4-(trifluoromethyl)-2-pyridinecarboxylate	[M+H] 528.3, 530.3 Rt=4.54min

321		Sodium 6-[2-(5-chloro-2-[(4-chloro-2-fluorophenyl)methyl]oxy]phenyl)-1-cyclopenten-1-yl]-4-(trifluoromethyl)-2-pyridinecarboxylate	[M+H] 526.3, 528.3 Rt=4.78min
322		Sodium 6-[2-(5-chloro-2-[(2,3,4-trifluorophenyl)methyl]oxy]phenyl)-1-cyclopenten-1-yl]-4-(trifluoromethyl)-2-pyridinecarboxylate	[M+H] 528.3, 530.3 Rt=4.58min
323		Sodium 6-[2-(5-chloro-2-[(3,4-difluorophenyl)methyl]oxy]phenyl)-1-cyclopenten-1-yl]-4-(trifluoromethyl)-2-pyridinecarboxylate	[M+H] 510.3, 512.3 Rt=4.49min
324		Sodium 6-[2-(5-chloro-2-[(3,4,5-trifluorophenyl)methyl]oxy]phenyl)-1-cyclopenten-1-yl]-4-(trifluoromethyl)-2-pyridinecarboxylate	[M+H] 528.3, 530.3 Rt=3.74min
325		Sodium 6-[2-(5-chloro-2-[(2,3-difluorophenyl)methyl]oxy]phenyl)-1-cyclopenten-1-yl]-4-(trifluoromethyl)-2-pyridinecarboxylate	[M+H] 510.3, 512.3 Rt=4.55min
326		Sodium 6-[2-(5-chloro-2-[(2-chloro-4-fluorophenyl)methyl]oxy]phenyl)-1-cyclopenten-1-yl]-4-(trifluoromethyl)-2-pyridinecarboxylate	[M+H] 526.3, 528.3 Rt=4.82min

327		Sodium 6-[2-(5-chloro-2-[(2,4,6-trifluorophenyl)methyl]oxyphenyl)-1-cyclopenten-1-yl]-4-(trifluoromethyl)-2-pyridinecarboxylate	[M+H] 528.3, 530.3 Rt=3.87min
328		sodium 5-[2-(5-bromo-2-[(2-fluorophenyl)methyl]oxyphenyl)-1-cyclopenten-1-yl]-2-(trifluoromethyl)-3-pyridinecarboxylate	Rt = 4.0min [M+H] 536, 539 (1Br)
329		sodium 5-[2-(5-bromo-2-[(4-fluorophenyl)methyl]oxyphenyl)-1-cyclopenten-1-yl]-2-(trifluoromethyl)-3-pyridinecarboxylate	Rt = 4.0min [M+H] 536, 539 (1Br)
330		sodium 5-[2-(5-bromo-2-[(2,4-difluorophenyl)methyl]oxyphenyl)-1-cyclopenten-1-yl]-2-(trifluoromethyl)-3-pyridinecarboxylate	Rt = 4.0min [M+H] 556, 557 (1Br)
331		sodium 5-[2-(5-bromo-2-[(2,4,6-trifluorophenyl)methyl]oxyphenyl)-1-cyclopenten-1-yl]-2-(trifluoromethyl)-3-pyridinecarboxylate	Rt = 3.9min [M+H] 574, 575 (1Br)
332		sodium 5-[2-(5-bromo-2-[(2-chloro-4-fluorophenyl)methyl]oxyphenyl)-1-cyclopenten-1-yl]-2-(trifluoromethyl)-3-pyridinecarboxylate	Rt = 4.3min [M+H] 572, 573 (1Br)

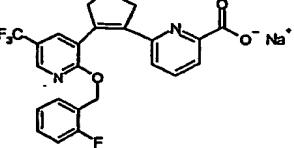
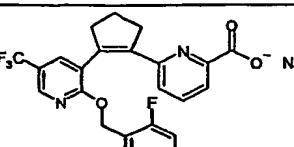
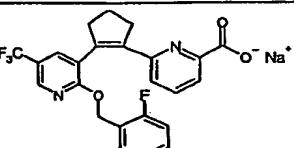
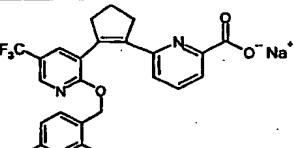
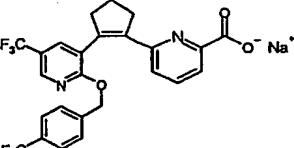
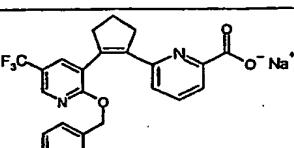
333		sodium 5-[2-(5-bromo-2-[(4-chlorophenyl)methyl]oxy)phenyl]-1-cyclopenten-1-yl]-2-(trifluoromethyl)-3-pyridinecarboxylate	Rt = 4.2min [M+H] 554, 556 (1Br)
334		sodium 6-(2-{4,5-dichloro-2-[(phenylmethyl)oxy]phenyl}-1-cyclopenten-1-yl)-2-pyridinecarboxylate	Rt=4.09 [MH+] 440.4, 442.4
335		sodium 6-[2-(4,5-dichloro-2-[(2-fluorophenyl)methyl]oxy)phenyl]-1-cyclopenten-1-yl]-2-pyridinecarboxylate	Rt=4.11 [MH+] 458.4, 460.4
336		sodium 6-[2-(4,5-dichloro-2-[(2,4-difluorophenyl)methyl]oxy)phenyl]-1-cyclopenten-1-yl]-2-pyridinecarboxylate	Rt=4.12 [MH+] 476.4, 478.4
337		sodium 6-[2-(4,5-dichloro-2-[(2,4,6-trifluorophenyl)methyl]oxy)phenyl]-1-cyclopenten-1-yl]-2-pyridinecarboxylate	Rt=4.14 [MH+] 494.4, 496.4
338		sodium 3-chloro-6-[2-[5-(trifluoromethyl)-2-([(4-(trifluoromethyl)phenyl)methyl]oxy)phenyl]-1-cyclopenten-1-yl]-2-pyridinecarboxylate	Rt = 4.41min [M+H] 542(1Cl)

339		5-(2-{5-Chloro-2-[(phenylmethyl)oxy]phenyl}-1-cyclopenten-1-yl)-3-pyridazinecarboxylic acid	[M+H] 407.2, 409.2 Rt=4.42min
340		5-[2-(5-Chloro-2-[(4-fluorophenyl)methyl]oxy)phenyl]-1-cyclopenten-1-yl]-3-pyridazinecarboxylic acid	[M+H] 425.1, 427.1 Rt=4.30min
341		5-[2-(5-Chloro-2-[(2,4-difluorophenyl)methyl]oxy)phenyl]-1-cyclopenten-1-yl]-3-pyridazinecarboxylic acid	[M+H] 443.1, 445.1 Rt=4.30min
342		Sodium 2-fluoro-5-[2-{[(phenylmethyl)oxy]-5-(trifluoromethyl)-3-pyridinyl}-1-cyclopenten-1-yl]benzoate	LC/MS: Rt = 4.41min. [MH ⁺] 458
343		Sodium 3-(2-{5-chloro-2-[(phenylmethyl)oxy]-3-pyridinyl}-1-cyclopenten-1-yl)-5-fluorobenzoate	LC/MS: Rt = 4.35min. [MH ⁺] 424, 426.
344		Sodium 5-[2-(5-chloro-2-[(2,4-difluorophenyl)methyl]oxy)-3-pyridinyl]-1-cyclopenten-1-yl]-2-fluorobenzoate	LC/MS: Rt = 4.42min. [MH ⁺] 460, 462.

345		Sodium 3-[2-(5-chloro-2-[(4-fluorophenyl)methyl]oxy)-3-pyridinyl]-1-cyclopenten-1-yl]-5-fluorobenzoate	LC/MS: Rt = 4.36min. [MH ⁺] 442, 444.
346		Sodium 3-[2-(5-chloro-2-[(2-fluorophenyl)methyl]oxy)-3-pyridinyl]-1-cyclopenten-1-yl]-5-fluorobenzoate	LC/MS: Rt = 4.41min. [MH ⁺] 442, 444.
347		Sodium 3-[2-(5-chloro-2-[(2,4-difluorophenyl)methyl]oxy)-3-pyridinyl]-1-cyclopenten-1-yl]-5-fluorobenzoate	LC/MS: Rt = 4.42min. [MH ⁺] 460, 462.
348		Sodium 3-[2-(5-chloro-2-[(2,6-difluorophenyl)methyl]oxy)-3-pyridinyl]-1-cyclopenten-1-yl]-5-fluorobenzoate	LC/MS: Rt = 4.35min. [MH ⁺] 460, 462.
349		Sodium 3-[2-(5-chloro-2-[(2,4,6-trifluorophenyl)methyl]oxy)-3-pyridinyl]-1-cyclopenten-1-yl]-5-fluorobenzoate	LC/MS: Rt = 4.39min. [MH ⁺] 478, 480.
350		Sodium 3-[2-(5-chloro-2-[(4-chloro-2-fluorophenyl)methyl]oxy)-3-pyridinyl]-1-cyclopenten-1-yl]-5-fluorobenzoate	LC/MS: Rt = 4.62min. [MH ⁺] 476, 477, 478, 479.

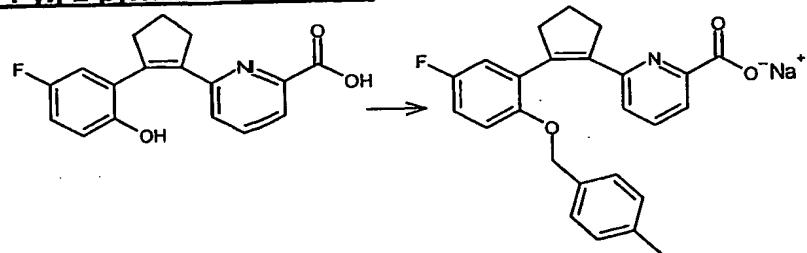
351		Sodium 3-[2-[5-chloro-2-((2-fluoro-4-(trifluoromethyl)phenyl)methoxy)-3-pyridinyl]-1-cyclopenten-1-yl]-5-fluorobenzoate	LC/MS: Rt = 4.56min. [MH ⁺] 508, 510.
352		Sodium 5-[2-[2-((2,4-difluorophenyl)methyl)oxy]-3-(trifluoromethyl)-3-pyridinyl]-1-cyclopenten-1-yl]-2-fluorobenzoate	LC/MS: Rt = 4.43min. [MH ⁺] 494.
353		Sodium 2-fluoro-5-[2-[4-(trifluoromethyl)phenyl]methoxy]-5-(trifluoromethyl)-3-pyridinyl]-1-cyclopenten-1-yl]benzoate	LC/MS: Rt = 4.30min. [MH ⁺] 476.
354		Sodium 5-[2-(2-((2,4-difluorophenyl)methyl)oxy)-3-pyridinyl]-1-cyclopenten-1-yl]-2-fluorobenzoate	LC/MS: Rt=4.20min [MH ⁺] 426.
355		Sodium 3-amino-5-[2-[(phenylmethyl)oxy]-5-(trifluoromethyl)-3-pyridinyl]-1-cyclopenten-1-yl]benzoate	¹ H NMR (MeOD) δ: 1.99-2.08(2H, m), 2.80-2.92(4H, m), 5.35(2H, s), 6.44(1H, t), 7.15(2H, dt), 7.23-7.35(5H, m), 7.51(1H, d), 8.27-8.29(1H,m). LC/MS Rt=3.71min [MH ⁺] 455.

356		Sodium 6-{2-[2-[(4-fluorophenyl)methyl]oxy]-5-(trifluoromethyl)-3-pyridinyl}-1-cyclopenten-1-yl]-2-pyridinecarboxylate	¹ H NMR (MeOD) δ: 2.03-2.11(2H, m), 2.86-2.91(2H, m), 3.08-3.13(2H, m), 5.31(2H, s), 6.79(1H, d), 7.03(2H, t), 7.26-7.30(2H, m), 7.44(1H, t), 7.61(1H, d), 7.72(1H, d), 8.34(1H, s). LC/MS Rt=3.88min [MH ⁺] 459.
357		Sodium 6-{2-[2-[(2-chloro-4-fluorophenyl)methyl]oxy]-5-(trifluoromethyl)-3-pyridinyl}-1-cyclopenten-1-yl]-2-pyridinecarboxylate	¹ H NMR (MeOD) δ: 2.03-2.11(2H, m), 2.85-2.90(2H, m), 3.08-3.13(2H, m), 5.38(2H, s), 6.81(1H, d), 7.15-7.20(2H, m), 7.25(1H, t), 7.46(1H, t), 7.63(1H, d), 7.72(1H, d), 8.35(1H, s). LC/MS Rt=4.07min [MH ⁺] 493.
358		Sodium 6-{2-[2-[(4-chlorophenyl)methyl]oxy]-5-(trifluoromethyl)-3-pyridinyl}-1-cyclopenten-1-yl]-2-pyridinecarboxylate	¹ H NMR (MeOD) δ: 2.04-2.12(2H, m), 2.87-2.92(2H, m), 3.09-3.14(2H, m), 5.31(2H, s), 6.80(1H, d), 7.23(2H, d), 7.29-7.34(2H, m), 7.45(1H, t), 7.63(1H, d), 7.72(1H, d), 8.34(1H, s). LC/MS Rt=4.04min [MH ⁺] 475.
359		Sodium 6-{2-[2-[(4-chloro-2-fluorophenyl)methyl]oxy]-5-(trifluoromethyl)-3-pyridinyl}-1-cyclopenten-1-yl]-2-pyridinecarboxylate	LC/MS: Rt=4.07min [MH ⁺] 493

360		Sodium 6-{2-[2-[(2-fluorophenyl)methyl]oxy]-5-(trifluoromethyl)-3-pyridinyl]-1-cyclopenten-1-yl}-2-pyridinecarboxylate	LC/MS: Rt=3.88min [MH ⁺] 459
361		Sodium 6-{2-[2-[(2,6-difluorophenyl)methyl]oxy]-5-(trifluoromethyl)-3-pyridinyl]-1-cyclopenten-1-yl}-2-pyridinecarboxylate	LC/MS: Rt=3.85min [MH ⁺] 477
362		Sodium 6-{2-[2-[(2-chloro-6-fluorophenyl)methyl]oxy]-5-(trifluoromethyl)-3-pyridinyl]-1-cyclopenten-1-yl}-2-pyridinecarboxylate	LC/MS: Rt=3.98min [MH ⁺] 493
363		Sodium 6-{2-[2-[(2,4-difluorophenyl)methyl]oxy]-5-(trifluoromethyl)-3-pyridinyl]-1-cyclopenten-1-yl}-2-pyridinecarboxylate	LC/MS: Rt=3.91min [MH ⁺] 477
364		Sodium 6-{2-[5-(trifluoromethyl)-2-((4-(trifluoromethyl)phenyl)methyl)oxy]-3-pyridinyl]-1-cyclopenten-1-yl}-2-pyridinecarboxylate	LC/MS: Rt=4.04min [MH ⁺] 509
365		Sodium 6-{2-[2-[(4-bromo-2-fluorophenyl)methyl]oxy]-5-(trifluoromethyl)-3-pyridinyl]-1-cyclopenten-1-yl}-2-pyridinecarboxylate	LC/MS: Rt=4.11min [MH ⁺] 537, 539

366		Sodium 6-[2-[2-((2,4,5-trifluorophenyl)methyl)oxy]-5-(trifluoromethyl)-3-pyridinyl]-1-cyclopenten-1-yl]-2-pyridinecarboxylate	LC/MS: Rt=4.07min [MH ⁺] 527
367		Sodium 6-[2-[2-((2,4,5-trifluorophenyl)methyl)oxy]-3-(trifluoromethyl)-2-pyridinyl]-1-cyclopenten-1-yl]-2-pyridinecarboxylate	LC/MS: Rt=3.94min [MH ⁺] 495
368		Sodium 6-[2-[2-((2,3,6-trifluorophenyl)methyl)oxy]-3-(trifluoromethyl)-2-pyridinyl]-1-cyclopenten-1-yl]-2-pyridinecarboxylate	LC/MS: Rt=3.87min [MH ⁺] 495

Example 369 Sodium 6-[2-(5-fluoro-2-{[(4-methylphenyl)methyl]oxy}phenyl]-1-cyclopenten-1-yl]-2-pyridinecarboxylate

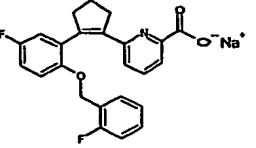
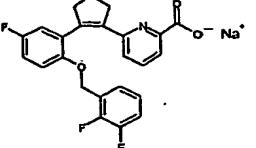
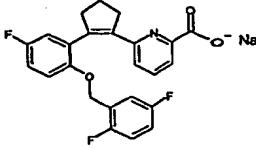
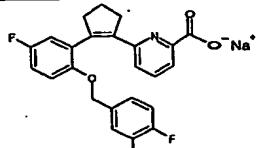
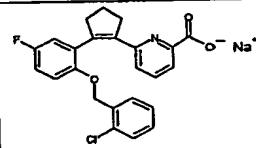
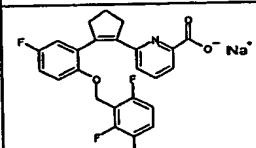
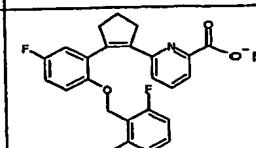
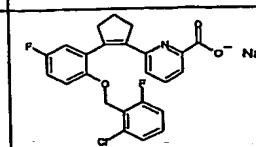


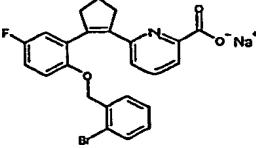
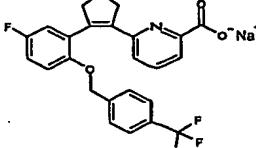
5 6-[2-[5-Fluoro-2-hydroxyphenyl]-1-cyclopenten-1-yl]-2-pyridinecarboxylic acid methyl ester (104mg, 0.333mmol) in dimethylformamide (4ml) was treated with 4-methylbenzyl bromide (66mg, 0.356mmol) and potassium carbonate (140mg, 1.0mmol). The reaction mixture was then refluxed overnight under nitrogen, filtered through celite and reduced under vacuum to an oil. The oil was dissolved in methanol (3ml), 2M sodium hydroxide (2ml) was added and the reaction mixture stirred at 65°C for one hour. The reaction mixture was then reduced down to ~1ml under vacuum, diluted to 20ml with water and extracted with ethyl acetate (2X20ml). The organic extract was then washed with brine (20ml), dried over sodium sulphate and evaporated down under reduced pressure to the required product (52mg, 36%). LC/MS Rt=3.73min [MH⁺] 404.

10 and the reaction mixture stirred at 65°C for one hour. The reaction mixture was then reduced down to ~1ml under vacuum, diluted to 20ml with water and extracted with ethyl acetate (2X20ml). The organic extract was then washed with brine (20ml), dried over sodium sulphate and evaporated down under reduced pressure to the required product (52mg, 36%). LC/MS Rt=3.73min [MH⁺] 404.

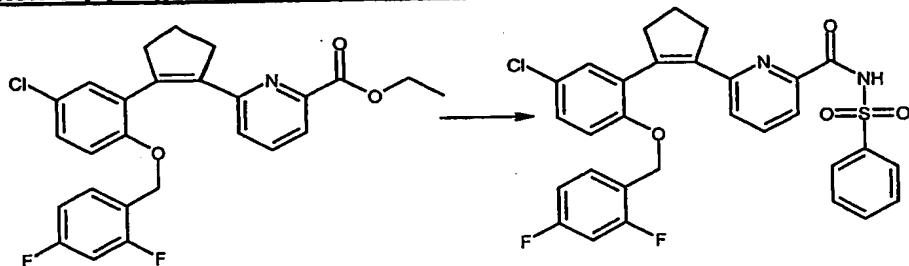
The following Examples were prepared by the procedure used for sodium 6-[2-(5-fluoro-2-{{(4-methylphenyl)methyl}oxy}phenyl)-1-cyclopenten-1-yl]-2-pyridinecarboxylate:

Example	Structure	Name	LC/MS
370		Sodium 6-[2-(2-{{(4-chlorophenyl)methyl}oxy}-5-fluorophenyl)-1-cyclopenten-1-yl]-2-pyridinecarboxylate	Rt = 3.83, [MH ⁺] 424
371		Sodium 6-[2-(5-fluoro-2-{{(2,4,6-trifluorophenyl)methyl}oxy}phenyl)-1-cyclopenten-1-yl]-2-pyridinecarboxylate	Rt = 3.58, [MH ⁺] 444
372		Sodium 6-[2-(5-fluoro-2-{{[2-fluoro-4-(trifluoromethyl)phenyl]methyl}oxy}phenyl)-1-cyclopenten-1-yl]-2-pyridinecarboxylate	Rt = 3.94, [MH ⁺] 476
373		Sodium 6-[2-(2-{{(4-chloro-2-fluorophenyl)methyl}oxy}-5-fluorophenyl)-1-cyclopenten-1-yl]-2-pyridinecarboxylate	Rt = 3.89, [MH ⁺] 442
374		Sodium 6-[2-(2-{{(4-bromophenyl)methyl}oxy}-5-fluorophenyl)-1-cyclopenten-1-yl]-2-pyridinecarboxylate	Rt = 3.90, [MH ⁺] 470
375		Sodium 6-[2-(2-{{(2-chloro-4-fluorophenyl)methyl}oxy}-5-fluorophenyl)-1-cyclopenten-1-yl]-2-pyridinecarboxylate	Rt = 3.88, [MH ⁺] 442

376		Sodium 6-[2-(5-fluoro-2-[(2-fluorophenyl)methyl]oxy)phenyl]-1-cyclopenten-1-yl]-2-pyridinecarboxylate	Rt = 3.57, [MH ⁺] 408
377		Sodium 6-[2-(2-[(2,3-difluorophenyl)methyl]oxy)-5-fluorophenyl]-1-cyclopenten-1-yl]-2-pyridinecarboxylate	Rt = 3.64, [MH ⁺] 426
378		Sodium 6-[2-(2-[(2,5-difluorophenyl)methyl]oxy)-5-fluorophenyl]-1-cyclopenten-1-yl]-2-pyridinecarboxylate	Rt = 3.67, [MH ⁺] 426
379		Sodium 6-[2-(2-[(3,4-difluorophenyl)methyl]oxy)-5-fluorophenyl]-1-cyclopenten-1-yl]-2-pyridinecarboxylate	Rt = 3.68, [MH ⁺] 426
380		Sodium 6-[2-(2-[(2-chlorophenyl)methyl]oxy)-5-fluorophenyl]-1-cyclopenten-1-yl]-2-pyridinecarboxylate	Rt = 3.84, [MH ⁺] 424
381		Sodium 6-[2-(5-fluoro-2-[(2,3,6-trifluorophenyl)methyl]oxy)-5-fluorophenyl]-1-cyclopenten-1-yl]-2-pyridinecarboxylate	Rt = 3.57, [MH ⁺] 444
382		Sodium 6-[2-(2-[(2,6-difluorophenyl)methyl]oxy)-5-fluorophenyl]-1-cyclopenten-1-yl]-2-pyridinecarboxylate	Rt = 3.49, [MH ⁺] 426
383		Sodium 6-[2-(2-[(2-chloro-6-fluorophenyl)methyl]oxy)-5-fluorophenyl]-1-cyclopenten-1-yl]-2-pyridinecarboxylate	Rt = 3.66, [MH ⁺] 442

384		Sodium 6-[2-(2-{[(2-bromophenyl)methyl]oxy}-5-fluorophenyl)-1-cyclopenten-1-yl]-2-pyridinecarboxylate	Rt = 3.90, [MH ⁺] 470
385		Sodium 6-[2-[5-fluoro-2-({[4-(trifluoromethyl)phenyl]methyl}oxy)phenyl]-1-cyclopenten-1-yl]-2-pyridinecarboxylate	Rt = 3.88, [MH ⁺] 458

Example 386 6-[2-(5-Chloro-2-{{(2,4-difluorophenyl)methyl}oxy}phenyl)-1-cyclopenten-1-yl]-N-(phenylsulfonyl)-2-pyridinecarboxamide

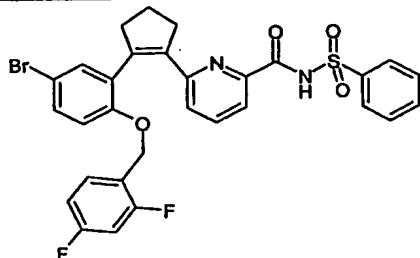


5 a) Ethyl 6-[2-(5-chloro-2-[(2,4-difluorophenyl)methyl]oxy)phenyl]-1-cyclopenten-1-yl]-2-pyridinecarboxylate (140mg, 0.30mmol) was dissolved in ethanol (5ml) and 2M sodium hydroxide (1ml) and heated to reflux then left to cool for 60 minutes. The solution was diluted with water then extracted with isohexane and acidified to pH4 with hydrochloric acid. The mixture was extracted with diethyl ether. The organic solution was dried over magnesium sulphate and evaporated to give 6-[2-(5-chloro-2-[(2,4-difluorophenyl)methyl]oxy)phenyl]-1-cyclopenten-1-yl]-2-pyridinecarboxylic acid (110mg). LC/MS Rt=3.88 [MH⁺] 442.3, 444.3.

10 b) A mixture of 6-[2-(5-chloro-2-[(2,4-difluorophenyl)methyl]oxy)phenyl]-1-cyclopenten-1-yl]-2-pyridinecarboxylic acid (110mg, 0.25mmol), benzenesulphonamide (58mg, 0.3mmol), 1-[3-(dimethylamino)propyl]-3-ethylcarbodiimide hydrochloride (58mg, 0.3mmol) and 4-dimethylaminopyridine (3mg, 0.025mmol) in 1:1 dichloromethane/tetrahydrofuran (4ml) was stirred at room temperature for 2 hours and more benzenesulphonamide (16mg, 0.1mmol), 1-[3-(dimethylamino)propyl]-3-ethylcarbodiimide hydrochloride (19mg, 0.1mmol) and 4-dimethylaminopyridine (1mg) was added. After a further 2 hours the mixture was diluted with ether/water and the organic layer dried (magnesium sulphate), evaporated and purified by chromatography on silica eluting with ethyl acetate/iso-hexane to give a white solid (85mg).

¹H NMR (CDCl₃) δ 2.07-2.14 (2H, m), 2.84-2.88 (2H, m), 2.98-3.01 (2H, m), 5.04 (2H, s), 6.74-6.79 (2H, m), 6.99 (1H, d), 7.06 (1H, d), 7.16-7.32 (3H, m), 7.54 (2H, t), 7.63 (2H, q), 7.81 (1H, d), 8.08-8.10 (2H, m), 9.55 (1H, s). LC/MS t=4.30, [MH⁺] 581.3, 583.3.

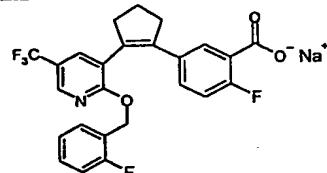
5 **Example 387 6-[2-(5-bromo-2-[(2,4-difluorophenyl)methoxy]phenyl)-1-cyclopenten-1-yl]-N-(phenylsulfonyl)-2-pyridinecarboxamide**



A mixture of 6-[2-(5-bromo-2-[(2,4-difluorophenyl)methoxy]phenyl)-1-cyclopenten-1-yl]-2-pyridinecarboxylic acid (110mg, 0.23 mmol), benzenesulphonamide(45mg, 0.29 mmol), 10 1-[3-(dimethylamino)propyl]-3-ethylcarbodiimide hydrochloride (55mg, 0.29mmol), and 4-dimethylaminopyridine (5mg) in 1:1 dichloromethane/tetrahydrofuran (5ml) was stirred at RT for 24 hours. The reaction mixture was diluted with diethyl ether (25ml) and washed with saturated sodium bicarbonate solution, water and brine. The organic phase was separated, dried and evaporated. Chromatography of the residue eluting with 1:9 ethyl acetate/hexane gave the title compound as a colourless solid (52mg).

15 LC/MS: Rt = 4.33 min. [M+H] = 625, 627.

Example 388 2-Fluoro-5-(2-[2-[(2-fluorophenyl)methoxy]-5-(trifluoromethyl)pyridin-3-yl]cyclopent-1-en-1-yl)-benzoic acid, sodium salt



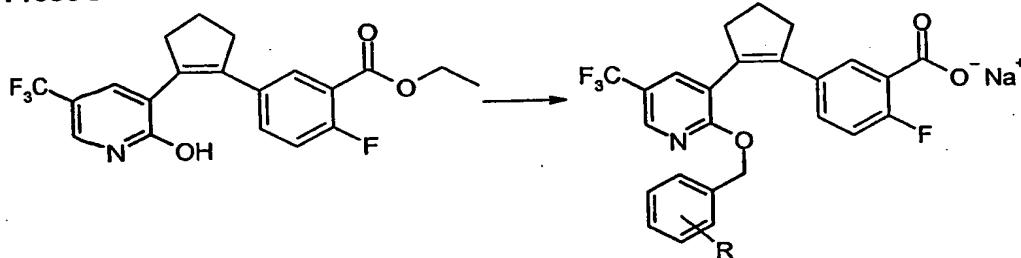
20 The corresponding ethyl ester was dissolved in ethanol (1ml) and 2M aqueous sodium hydroxide (1ml) was added. The mixture was heated to 120°C, by microwave, for 3mins. The reaction mixture was concentrated *in vacuo*, and the residue partitioned between ethyl acetate and water. The organic extract was dried (Na₂SO₄) and concentrated *in vacuo* to give the title compound as the sodium salt. LC/MS Rt=4.07min [MH⁺] 477.

The following compounds were prepared as their sodium salts by the same method, starting from the appropriate ethyl esters.

Example	Structure	COMPOUND NAME	LCMS
389		5-(2-{[2,6-Difluorophenyl]methoxy}-5-(trifluoromethyl)pyridin-3-yl)cyclopent-1-en-1-yl)-2-fluorobenzoic acid, sodium salt	Rt= 4.03min [MH ⁺] 495
390		5-(2-{[2-Chloro-4-fluorophenyl]methoxy}-5-(trifluoromethyl)pyridin-3-yl)cyclopent-1-en-1-yl)-2-fluorobenzoic acid, sodium salt	Rt= 4.25min [MH ⁺] 512

5

General Procedure C



Ethyl 2-fluoro-5-{2-[2-hydroxy-5-(trifluoromethyl)pyridin-3-yl]cyclopent-1-en-1-yl}benzoate (250mg, 0.63mmol) was dissolved in toluene (3ml), together with silver carbonate (192mg, 0.70mmol) and a substituted benzyl bromide (1.1equiv.). The mixture was heated to reflux 10 for 4 hours, then concentrated *in vacuo*, and the product taken on without further purification.

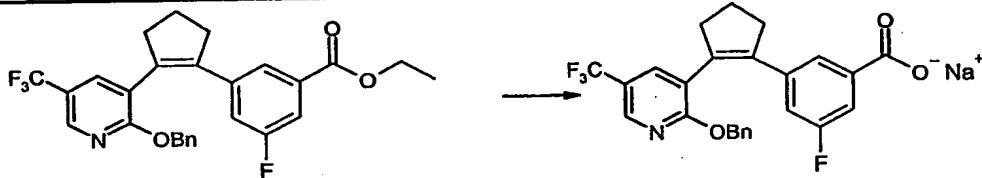
Each residue was dissolved in a mixture of ethanol (2ml) and 2N aqueous sodium 15 hydroxide (2ml), and this mixture was heated to 120°C, by microwave, for 3mins. The reaction mixture was filtered and concentrated *in vacuo*. The residue was dissolved in dichloromethane and treated with acetic acid, and then again concentrated *in vacuo*. The resulting material was purified using a basic solid phase extraction cartridge (Isolute® Flash NH₂), loading the crude material as a methanol solution, and eluting with 10% aqueous HCl in methanol. The resulting acids were redissolved in dichloromethane and 20 treated with aqueous 2N sodium hydroxide. The layers were separated, and the organic layer was concentrated *in vacuo*. The resulting sodium salt was redissolved in dioxane, which was removed by freeze-drying to give the product (sodium salt) as a solid.

The following compounds were prepared by General Procedure C:

Examples	Structure	Compound Name	LCMS
391		2-Fluoro-5-(2-{(trifluoromethyl)-2-[(2,4,6-trifluorophenyl)methoxy]pyridin-3-yl}cyclopent-1-en-1-yl)-benzoic acid, sodium salt	Rt= 4.07min [MH ⁺] 512
392		2-Fluoro-5-(2-{(trifluoromethyl)-2-[(2,4,5-trifluorophenyl)methoxy]pyridin-3-yl}cyclopent-1-en-1-yl)-benzoic acid, sodium salt	Rt= 4.09min [MH ⁺] 512
393		2-Fluoro-5-(2-{(trifluoromethyl)-2-[(2,3,6-trifluorophenyl)methoxy]pyridin-3-yl}cyclopent-1-en-1-yl)-benzoic acid, sodium salt	Rt= 4.11min [MH ⁺] 512
394		2-Fluoro-5-[2-(5-(trifluoromethyl)-2-[[4-(trifluoromethyl)phenyl]methoxy]pyridin-3-yl)cyclopent-1-en-1-yl]-benzoic acid, sodium salt	Rt= 4.19min [MH ⁺] 526

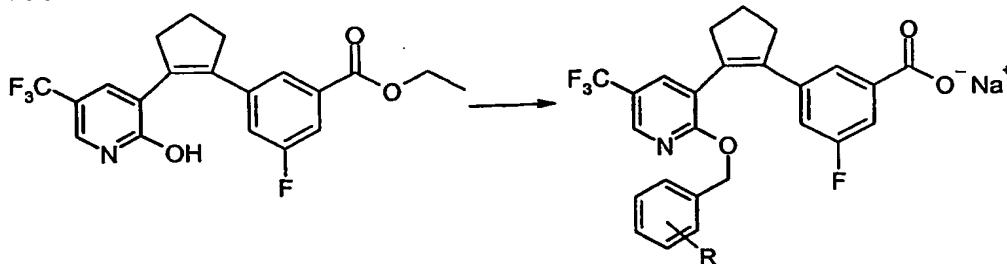
395		2-Fluoro-5-[2-(2-[2-fluoro-4-(trifluoromethyl)phenyl]methoxy)-5-(trifluoromethyl)pyridin-3-yl]cyclopent-1-en-1-yl]-benzoic acid, sodium salt	Rt= 4.28min [MH ⁺] 544
396		5-(2-{2-[(2-Chloro-6-fluorophenyl)methoxy]-5-(trifluoromethyl)pyridin-3-yl}cyclopent-1-en-1-yl)-2-fluorobenzoic acid, sodium salt	Rt= 4.16min [MH ⁺] 510
397		5-(2-{2-[(4-Bromo-2-fluorophenyl)methoxy]-5-(trifluoromethyl)pyridin-3-yl}cyclopent-1-en-1-yl)-2-fluorobenzoic acid, sodium salt	Rt= 4.28min [MH ⁺] 554,556

Example 398 3-Fluoro-5-{2-[2-(phenylmethoxy)-5-(trifluoromethyl)pyridin-3-yl]cyclopent-1-en-1-yl}benzoic acid, sodium salt



5 Ethyl 2-fluoro-5-{2-[2-(phenylmethoxy)-5-(trifluoromethyl)pyridin-3-yl]cyclopent-1-en-1-yl}benzoate (150mg, 0.31mmol) was dissolved in ethanol (2ml) and 2M sodium hydroxide (1.0ml) was added. The mixture was heated to reflux for 1 hour, by which time TLC analysis indicated that the reaction was complete. The cooled reaction mixture was diluted with water, acidified to pH5 with acetic acid, and then extracted with diethyl ether (x2). The combined organic extracts were washed with water, dried (Na_2SO_4) and concentrated *in vacuo* to give the crude acid, which was further purified by HPLC. The acid was treated with 2M aqueous sodium hydroxide, and this mixture extracted with dichloromethane. The organic extracts were concentrated *in vacuo* to give the title compound as the sodium salt. LC/MS Rt=4.22min [MH⁺] 458.

10 15 ¹H NMR (MeOD) δ : 2.06-2.14(2H, m), 2.86-2.97(4H, m), 5.31(2H, s), 6.93(1H, ddd), 7.17-7.21(2H, m), 7.24-7.30(3H, m), 7.43(1H, ddd), 7.51(1H, t), 7.68(1H, d), 8.38(1H, dd).

General Procedure D

5 Ethyl 3-fluoro-5-{2-[2-hydroxy-5-(trifluoromethyl)pyridin-3-yl]cyclopent-1-en-1-yl}benzoate (250mg, 0.63mmol) was dissolved in toluene (3ml), together with silver carbonate (192mg, 0.70mmol) and a substituted benzyl bromide (1.1equiv.). The mixture was heated to reflux for 4 hours, then concentrated *in vacuo*, and the product taken on without further purification.

10 Each residue was dissolved in a mixture of ethanol (2ml) and 2N aqueous sodium hydroxide (2ml), and this mixture was heated to 120°C, by microwave, for 3mins. The reaction mixture was filtered and concentrated *in vacuo*. The residue was dissolved in dichloromethane and treated with acetic acid, and then again concentrated *in vacuo*. The resulting material was purified using a basic solid phase extraction cartridge (Isolute® Flash NH₂), loading the crude material as a methanol solution, and eluting with 10% aqueous HCl in methanol. The resulting acid was redissolved in dichloromethane and treated with aqueous 2N sodium hydroxide. The layers were separated, and the organic layer was concentrated *in vacuo*. This was followed by further purification by HPLC. The pure acid was treated with 2M aqueous sodium hydroxide, and the mixture extracted with dichloromethane. The organic extracts were concentrated *in vacuo* to give the title compound as the sodium salt.

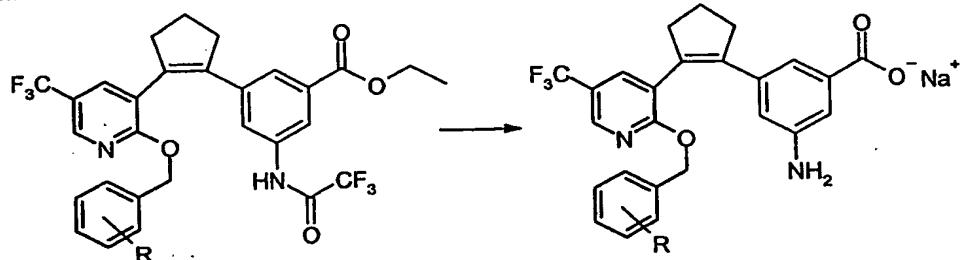
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The following Examples were prepared by General Procedure D:

Example	Structure	Compound Name	LCMS
399		3-Fluoro-5-(2-{(4-fluorophenyl)methoxy}-5-(trifluoromethyl)pyridin-3-yl)cyclopent-1-en-1-yl benzoic acid, sodium salt	Rt= 4.15min [MH ⁺] 476
400		5-(2-{(2,4-Difluorophenyl)methoxy}-5-(trifluoromethyl)pyridin-3-yl)cyclopent-1-en-1-yl 3-fluorobenzoic acid, sodium salt	Rt= 4.17min [MH ⁺] 494

401		5-(2-{2-[4-Chloro-2-fluorophenyl)methoxy]-5-(trifluoromethyl)pyridin-3-yl}cyclopent-1-en-1-yl)-3-fluorobenzoic acid, sodium salt	Rt= 4.31min [MH ⁺] 510
402		3-Fluoro-5-(2-{5-(trifluoromethyl)-2-[(2,4,6-trifluorophenyl)methoxy]pyridin-3-yl)cyclopent-1-en-1-yl}-benzoic acid, sodium salt	Rt= 4.12 min [MH ⁺] 512
403		5-(2-{2-[4-Bromo-2-fluorophenyl)methoxy]-5-(trifluoromethyl)pyridin-3-yl}cyclopent-1-en-1-yl)-3-fluorobenzoic acid, sodium salt	Rt= 4.40min [MH ⁺] 554, 556
404		Sodium 3-{2-[2-{[(2,6-difluorophenyl)methyl]oxy}-5-(trifluoromethyl)-3-pyridinyl]-1-cyclopenten-1-yl}-5-fluorobenzoate	Rt= 4.12min [MH ⁺] 493

General Procedure E

The ester was dissolved in ethanol (2ml) and 2M aqueous sodium hydroxide (1ml) was added. The mixture was heated to reflux for 2 hours. The reaction mixture was concentrated *in vacuo*, and treated according to procedure A or B.

Procedure A: The residue was triturated with aqueous sodium hydroxide to give the sodium salt as a solid, which was collected by filtration and washed with water.

Procedure B: The residue was partitioned between ethyl acetate and water. The organic layer was dried (Na_2SO_4), and concentrated *in vacuo*, to give the sodium salt as a glassy solid.

The following Examples were prepared as their sodium salts by General Procedure E, starting from the appropriate ethyl esters

Example	Structure	Compound Name	LCMS
405		3-Amino-5-(2-{2-[{(4-fluorophenyl)methoxy]-5-(trifluoromethyl)pyridin-3-yl}cyclopent-1-en-1-yl}-benzoic acid, sodium salt	Rt= 3.80min [MH ⁺] 473
406		3-Amino-5-(2-{2-[{(2,4-difluorophenyl)methoxy]-5-(trifluoromethyl)pyridin-3-yl}cyclopent-1-en-1-yl}-benzoic acid, sodium salt	Rt= 3.84min [MH ⁺] 491
407		3-Amino-5-(2-{2-[{(2-fluorophenyl)methoxy]-5-(trifluoromethyl)pyridin-3-yl}cyclopent-1-en-1-yl}-benzoic acid, sodium salt	Rt= 3.80min [MH ⁺] 473
408		3-Amino-5-(2-{2-[{(2,6-difluorophenyl)methoxy]-5-(trifluoromethyl)pyridin-3-yl}cyclopent-1-en-1-yl}-benzoic acid, sodium salt	Rt= 3.77min [MH ⁺] 491
409		3-Amino-5-(2-{2-[{(2-chloro-4-fluorophenyl)methoxy]-5-(trifluoromethyl)pyridin-3-yl}cyclopent-1-en-1-yl}-benzoic acid, sodium salt	Rt= 3.98min [MH ⁺] 507
410		3-Amino-5-(2-{2-[{(4-chloro-2-fluorophenyl)methoxy]-5-(trifluoromethyl)pyridin-3-yl}cyclopent-1-en-1-yl}-benzoic acid, sodium salt	Rt= 3.98min [MH ⁺] 507

411		3-Amino-5-(2-{5-(trifluoromethyl)-2-[(2,4,6-trifluorophenyl)methoxy]pyridin-3-yl}cyclopent-1-en-1-yl)-benzoic acid, sodium salt	Rt= 3.84min [MH ⁺] 509
412		3-Amino-5-(2-{5-(trifluoromethyl)-2-[(2,4,5-trifluorophenyl)methoxy]pyridin-3-yl}cyclopent-1-en-1-yl)-benzoic acid, sodium salt	Rt= 3.87min [MH ⁺] 509
413		3-Amino-5-(2-{5-(trifluoromethyl)-2-[(2,3,6-trifluorophenyl)methoxy]pyridin-3-yl}cyclopent-1-en-1-yl)-benzoic acid, sodium salt	Rt= 3.85min [MH ⁺] 509
414		3-Amino-5-[2-(5-(trifluoromethyl)-2-[(4-(trifluoromethyl)phenyl)methoxy]pyridin-3-yl)cyclopent-1-en-1-yl]-benzoic acid, sodium salt	Rt= 4.01min [MH ⁺] 523
415		3-Amino-5-[2-(2-[[2-fluoro-4-(trifluoromethyl)phenyl]methoxy]-5-(trifluoromethyl)pyridin-3-yl)cyclopent-1-en-1-yl]-benzoic acid, sodium salt	Rt= 4.01min [MH ⁺] 541
416		3-Amino-5-(2-[(2-chloro-6-fluorophenyl)methoxy]-5-(trifluoromethyl)pyridin-3-yl)cyclopent-1-en-1-yl]-benzoic acid, sodium salt	Rt= 3.89min [MH ⁺] 507

417		3-Amino-5-(2-{2-[(4-bromo-2-fluorophenyl)methoxy]-5-(trifluoromethyl)pyridin-3-yl}cyclopent-1-en-1-yl)-benzoic acid, sodium salt	Rt= 4.03min $[MH^+]$ 551, 553
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It is to be understood that the present invention covers all combinations of particular and preferred subgroups described herein above.

5

ASSAYS FOR DETERMINING BIOLOGICAL ACTIVITY

The compounds of formula (I) can be tested using the following assays to demonstrate their prostanoid antagonist or agonist activity in vitro and in vivo and their selectivity. The prostaglandin receptors investigated are DP, EP₁, EP₂, EP₃, EP₄, FP, IP and TP.

10

The ability of compounds to antagonise EP₁ & EP₃ receptors may be demonstrated using a functional calcium mobilisation assay. Briefly, the antagonist properties of compounds are assessed by their ability to inhibit the mobilisation of intracellular calcium ($[Ca^{2+}]_i$) in

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response to activation of EP₁ or EP₃ receptors by the natural agonist hormone prostaglandin E₂ (PGE₂). Increasing concentrations of antagonist reduce the amount of calcium that a given concentration of PGE₂ can mobilise. The net effect is to displace the PGE₂ concentration-effect curve to higher concentrations of PGE₂. The amount of calcium produced is assessed using a calcium-sensitive fluorescent dye such as Fluo-3, AM and a suitable instrument such as a Fluorimetric Imaging Plate Reader (FLIPR). Increasing amounts of $[Ca^{2+}]_i$ produced by receptor activation increase the amount of fluorescence produced by the dye and give rise to an increasing signal. The signal may be detected using the FLIPR instrument and the data generated may be analysed with suitable curve-fitting software.

25

The human EP₁ or EP₃ calcium mobilisation assay (hereafter referred to as 'the calcium assay') utilises Chinese hamster ovary-K1 (CHO-K1) cells into which a stable vector containing either EP₁ or EP₃ cDNA has previously been transfected. Cells are cultured in suitable flasks containing culture medium such as DMEM:F-12 supplemented with 10% v/v foetal calf serum, 2mM L-glutamine, 0.25mg/ml geneticin and 10µg/ml puromycin.

30

For assay, cells are harvested using a proprietary reagent that dislodges cells such as Versene. Cells are re-suspended in a suitable quantity of fresh culture media for introduction into a 384-well plate. Following incubation for 24 hours at 37°C the culture media is replaced with a medium containing fluo-3 and the detergent pluronic acid, and a further incubation takes place. Concentrations of compounds are then added to the plate in order to construct concentration-effect curves. This may be performed on the FLIPR in

order to assess the agonist properties of the compounds. Concentrations of PGE₂ are then added to the plate in order to assess the antagonist properties of the compounds.

The data so generated may be analysed by means of a computerised curve-fitting routine.

5 The concentration of compound that elicits a half-maximal inhibition of the calcium mobilisation induced by PGE₂ (pIC_{50}) may then be estimated.

Binding Assay for the Human Prostanoid EP₁ Receptor

10 Competition assay using [³H]-PGE2.

Compound potencies are determined using a radioligand binding assay. In this assay compound potencies are determined from their ability to compete with tritiated prostaglandin E₂ ([³H]-PGE₂) for binding to the human EP₁ receptor.

15 This assay utilises Chinese hamster ovary-K1 (CHO-K1) cells into which a stable vector containing the EP₁ cDNA has previously been transfected. Cells are cultured in suitable flasks containing culture medium such as DMEM:F-12 supplemented with 10% v/v foetal calf serum, 2mM L-glutamine, 0.25mg/ml geneticin, 10µg/ml puromycin and 10µM indomethacin.

20 Cells are detached from the culture flasks by incubation in calcium and magnesium free phosphate buffered saline containing 1 mM disodium ethylenediaminetetraacetic acid (Na₂EDTA) and 10µM indomethacin for 5 min. The cells are isolated by centrifugation at 250xg for 5mins and suspended in an ice cold buffer such as 50 mM Tris, 1mM Na₂EDTA, 140mM NaCl, 10µM indomethacin (pH 7.4). The cells are homogenised using a Polytron tissue disrupter (2x10s burst at full setting), centrifuged at 48,000xg for 20mins and the pellet containing the membrane fraction is washed three times by suspension and centrifugation at 48,000xg for 20mins. The final membrane pellet is suspended in an assay buffer such as 10mM 2-[N-morpholino]ethanesulphonic acid, 1mM Na₂EDTA, 10mM MgCl₂ (pH 6). Aliquots are frozen at -80°C until required.

25 For the binding assay the cell membranes, competing compounds and [³H]-PGE₂ (3nM final assay concentration) are incubated in a final volume of 100µl for 30 min at 30°C. All reagents are prepared in assay buffer. Reactions are terminated by rapid vacuum filtration over GF/B filters using a Brandell cell harvester. The filters are washed with ice cold assay buffer, dried and the radioactivity retained on the filters is measured by liquid scintillation counting in Packard TopCount scintillation counter.

30 40 The data are analysed using non linear curve fitting techniques (GraphPad Prism 3) to determine the concentration of compound producing 50% inhibition of specific binding (IC_{50}).

By application of the binding assay technique, compounds of the examples had an antagonist pIC₅₀ value of 6.0 to 9.5 at EP₁ receptors. Compounds of the examples had a pIC₅₀ value of < 6.0 at EP₃ receptors when measured by the calcium mobilisation assay.

- 5 No toxicological effects are indicated/expected when a compound (of the invention) is administered in the above mentioned dosage range.
The application of which this description and claims forms part may be used as a basis for priority in respect of any subsequent application. The claims of such subsequent
- 10 application may be directed to any feature or combination of features described herein. They may take the form of product, composition, process, or use claims and may include, by way of example and without limitation the following claims: